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DR. RICHARD M. PEARCE, *President.*

YAWS.
WITH A DEMONSTRATION OF INFECTED TISSUE.*

HENRY J. NICHOLS,
Captain, Medical Corps, U. S. A.

The discovery of the cause of syphilis by Schaudinn had an important sequel for tropical medicine in the discovery of the cause of yaws by Castellani in the same year, 1905. Castellani[1] says that in February of that year while examining smears from a case of yaws at Colombo in Ceylon, he found two kinds of spirochetes, one fairly large and one almost invisible with a strong Leishman stain. He paid little attention to them at the time, however, because he also found numbers of bacteria and undetermined oval bodies. You will recall that Schaudinn[2] found living spirochetes from a syphilitic lesion on March 3, 1905, that he stained these organisms wtih Giemsa's stain and that the report of Schaudinn and Hoffman appeared in May, 1905. After reading this report Castellani again took up the examination, also using Giemsa's stain, and again in a number of cases found the same tenuous spirochete which he considered morphologically identical with *Spirochæta pallida* and named *Spirochæta pertenuis* or *pallidula.* He sent slides to Schaudinn, who found besides two kinds of large spirochetes, one which he too considered morphologically identical with *Sp. pallida.* Castellani made a tentative report in June and also in November, 1905. Meanwhile Wellman[3] had at about the same time found in one case spirochetes, which he at first mistook for spirilla of relapsing fever, in serum from a yaw; no such organisms, however, were found in three other cases of yaws.

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*Read before the New York Pathological Society February 9, 1910. Published by permission of the Surgeon General, U. S. Army.

Castellani inoculated three monkeys, and in one, after sixteen days at the site of inoculation, a yaw-like lesion developed which repeatedly showed *Treponema pertenuis.* Later he developed the subject more fully.

Castellani's observations have been fully confirmed and extended in various parts of the world, particularly in Java and the Philippine Islands, so that it is now as certain that yaws is due to a spirochete as that syphilis is.

The finding of an organism in yaws which both Schaudinn and Castellani considered morphologically identical with *Spirochæta pallida* naturally raised the old question about the identity of the two diseases. As you doubtless recall, Hutchinson[4] has a theory that yaws is the original form of syphilis which has become modified by passage through the Caucasian race. To Hutchinson and his followers the finding of the spirochetes seemed to clinch the matter; but without reviewing all the evidence at present it may be said that everyone who has worked with the disease recently believes that yaws is not syphilis; as Castellani puts it, yaws is not syphilis any more than leprosy is tuberculosis.

The infectious nature of yaws has been known for a long time. Manson[5] says that the planters in the West Indies had yaw houses and other repressive measures to keep the disease under. Paulet[6], in 1848, inoculated seventeen negroes, all of whom developed the disease in twelve to twenty days; in thirteen cases the disease developed at the site of inoculation, in the other four cases it was generalized. Charlouis[7], a military surgeon in Batavia, in 1881 autoinoculated four cases and three developed additional yaws. He inoculated thirty-two Chinese prisoners and twenty-eight became infected. He then took a case of yaws in a Malay, explained the dangers of syphilis and proposed inoculation; the man agreed, and he produced a chancre on the chest, followed by a secondary eruption and glandular enlargement. Yaws and syphilis have been observed clinically in the same person at the same time in several instances.

Yaws has been studied experimentally in monkeys by Castellani[1], by Baerman and Halberstädter[8] of Neisser's expedition to Java, and by Ashburn and Craig[9] of the U. S. Army Board for the Study of Tropical Diseases as they exist in the Philippine Islands. As a result of their work we can formulate the following statements:

1. Yaws can be transmitted from man to monkey; from monkey to monkey, and from one part of the body to another; the serum from the yaws, the blood, the lymphatic glands, the spleen pulp and bone marrow may be infectious; the spinal fluid is not infectious; filtered fluids and extracts are not infectious.

2. In the monkey as in man the lesions are usually confined to the site of inoculation or the immediate region by autoinoculation; a general eruption may, however, occur.

3. Syphilis can be inoculated in an animal with yaws and vice versa. Castellani claims that he could demonstrate specific antigen and antibodies for yaws distinct from those of syphilis.

Histologically a yaw consists in an overgrowth and down-growth of the epithelial layers of the skin with edema and cellular infiltration of the corium, which together make a rounded mass of oozing papillæ. The treponema are found only among the degenerated epithelial downgrowths; there is no perivascular infiltration, there are no giant cells and there is very little reaction of the fixed connective tissue cells.

Although Schaudinn and Castellani found no morphological difference between *Treponema pertenuis* and *pallida*, Prowazek[10] believes that there are certain general differences between them. Major Russell[11] has also studied the two organisms and agrees with Prowazek. These differences which can be best shown in the slides are as follows:

Treponema pertenuis is slightly thicker and less rigid; the twists are not so regular; there is more tendency for the ends to curl up; the forms with longitudinal divisions are more numerous.

As a summary we may say that yaws is usually a localized disease of the skin and is spread by autoinoculation; general infection with general eruption may, however, occur. The following is a brief clinical description based on observations controlled by experiments.

Yaws is common on the west coast of Africa, in the West Indies and in the islands of the far East, from Ceylon to Samoa. Manson[5] believes it probable that it was brought to the West Indies from Africa by the slaves. It is described by travelers as far back as 1567 as the pox.

There is but one lesion, the yaw or raspberry-like growth on the skin. Initial lesions and sequelæ, such as ulcers, have been described by the older writers, but these views have not been substantiated. It is essentially a disease of childhood; in some places in the Philippines, as among the Moros who live in a communal system, practically every child has it, like measles among us. Daniels[5] says that in Fiji children who do not take the disease are inoculated by their parents, who regard an attack of yaws as more or less necessary and wholesome.

In children then we find these "fungoid excrescences" covered by a yellow crust of dried serum in various parts of the body, usually following autoinoculation from some other yaw, but occasionally occurring in definite crops. There may be a general glandular involvement, but there are no definite constitutional symptoms. The disease lasts a few months and gradually disappears.

In adults there may be pains in the joints and bones and loss of weight. Many of the cases in adults come from children by direct contact; for example, I have seen a mother with a yaw on her flank from carrying astride her hip her child whose buttocks were affected; again, a yaw on the breast from suckling a child whose lips were covered with yaws; and several grandfathers with a few yaws on the neck or head from carrying children. The same kind of contact infection probably occurs from child to child, although it is possible that flies and other insects may carry the organisms. To illustrate contact infection: several of us a short time ago made a medical survey of a typical Filipino town and found all the cases of yaws in groups. For example, in one house, two cases, child, age three, and grandfather, age seventy, with history of a third; in the next house, one case, child, age two; in the next house two cases, child, age two, mother, age twenty-five; and no other cases anywhere in the neighborhood. Sexual infection is very rare indeed; the only case at all suggestive was that of a prostitute with a yaw on the labium.

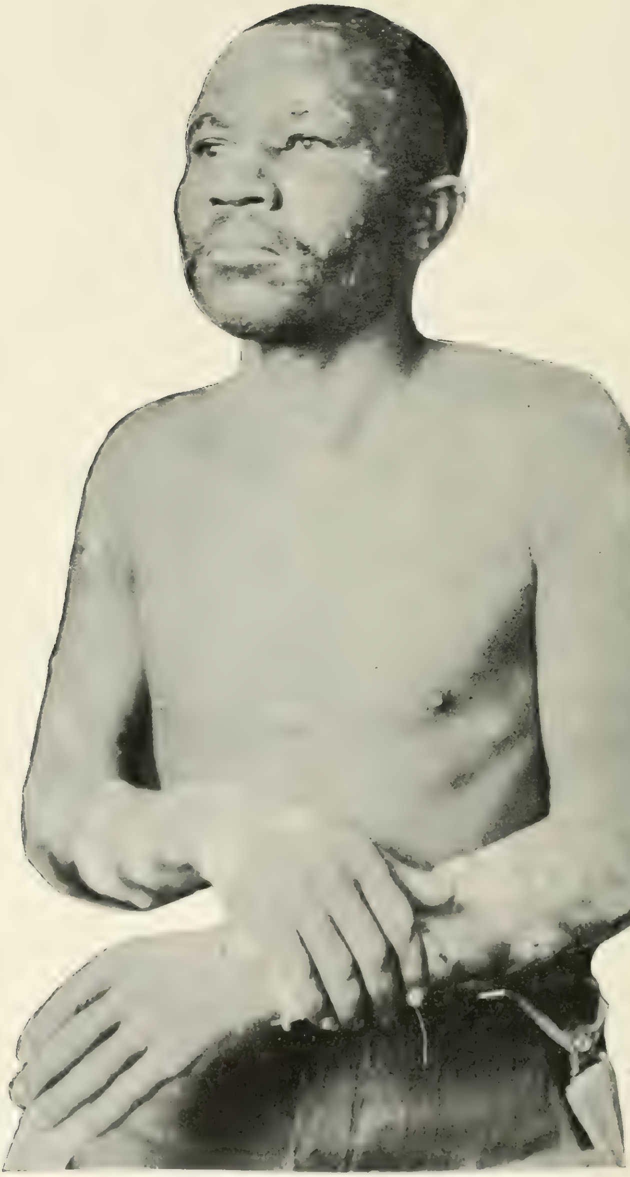
The evidence against the identity of the disease with syphilis is as follows:

1. Geographical distribution; yaws is confined to certain tropical regions; it exists where there is no syphilis, and has also died out while syphilis remained.

2. Yaws and syphilis may occur in the same person, and there is no immunity from one disease to the other.

3. The lesions in yaws are always the same, not pleomorphic.

4. The lesions of yaws affect principally the epithelial, not the connective tissue.



Yaws in colored soldier; showing second crop of lesions, smooth white patches of healed yaws and circular outline of granulation in still active yaws.

5. Yaws is principally a disease of children; but is neither hereditary nor congenital.

6. The lesions are extragenital and sexual transmission is practically unknown.

7. Constitutional symptoms are not the rule in yaws.

8. The treponemas may differ morphologically.

The occasion for the present paper is the occurrence of a well marked case of yaws in a colored soldier who returned from the Philippines last summer.

J. F.: Corporal, 10th Cavalry; age forty years. Family history is good; there is no evidence of syphilis.

Patient had measles and mumps in childhood, gonorrhea in 1907; emphatically denies any other venereal disease. He has been in the army eighteen years and was in the Philippine Islands in 1901-3 and 1907-9. He left Manila on May 15, 1909, in good condition; was exposed to venereal disease on May 12, in a small town near Fort McKinley, where he was stationed. He has seen yaws among native children, but did not come in contact with any cases as far as he knows.

The transport came home by the Suez Canal, arriving about July 25. While on board, about June 1, he developed pains in the chest and later in the joints, which became so severe that he was taken into the hospital for the last three weeks of the trip. The transport touched at Singapore, Colombo, and Aden; but there is no poetical fitness in the stop at Ceylon, as the men were not allowed ashore. The patient went ashore only once at Aden for about two hours, and had nothing to do with any of its people. After reaching New York, on July 25, he went to Fort Ethan Allen, Vermont, and entered the hospital immediately with the same vague rheumatic pains. On August 10, he noticed a small lump or pimple on his left cheek, and three days later a general eruption of the same kind on his back, chest, arms, legs, hands and feet. The lesion started as a papule, increased gradually, and became covered with a yellow crust which covered an oozing granulation. The medical officers in charge suspected yaws and gave him potassium iodide and yellow iodide of mercury, under which his pains improved and the lesions gradually dried up, until at the end of about six weeks he was entirely well. About four days later, October 2, a second crop of the same sort of lesions appeared on his face, arms and legs.

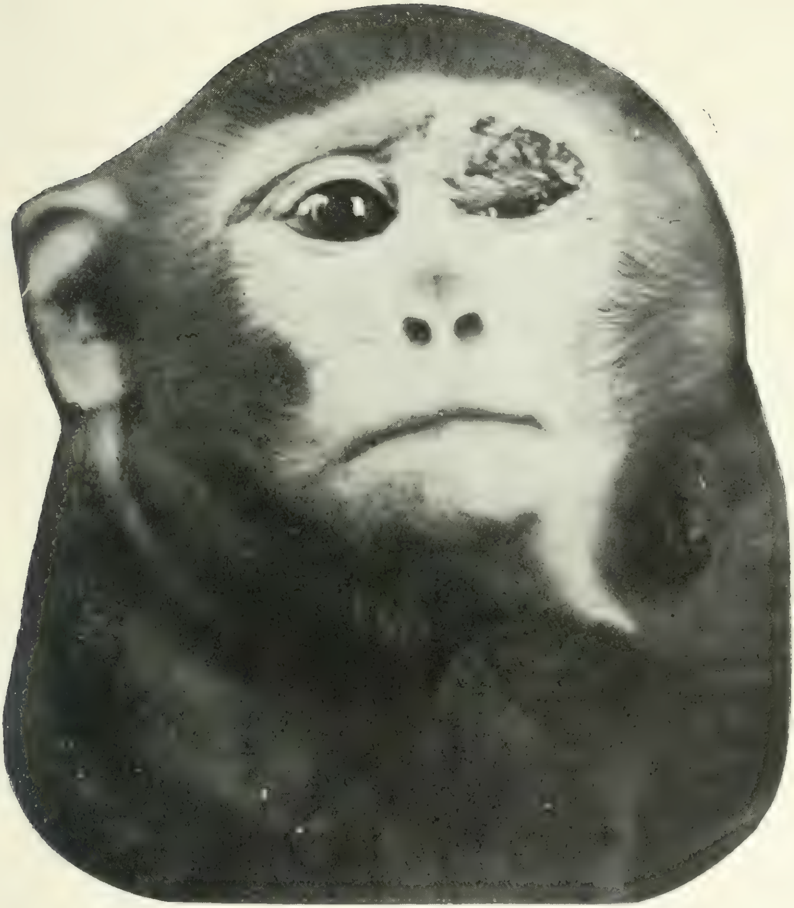
On December 9, he was transferred to Governor's Island by direction of the Surgeon-General for observation by Capt. J. F. Siler, who is giving a course in Tropical Medicine at the Post-Graduate School.

I saw the patient in December, and he was then recovering from a typical attack of yaws. Most of the yaws were nearly gone, but he still had several typical fungoid excrescences with a yellow crust. The papillæ were rather drier and more fibrous than is usual. He had a general glandular involvement and complained of pains and swelling in the ankles and knees and loss of weight. On two examinations treponemas were found in the serum from the yaws, by the dark field microscope.

He had been treated with mercury and potassium iodide; this treatment was changed to atoxyl, and in a few weeks his skin was entirely clear, except for white patches marking the site of the previous eruption of yaws. About a week ago a third crop of yaws broke out on his arms and legs; these are small and are already retrogressing. He is again on atoxyl.

On December 17, I took the patient to the Rockefeller Institute and excised a piece of one of the yaws, which Dr. Flexner rubbed into a slightly abraded surface over a rhesus monkey's eyebrow. The primary abrasion healed completely, but twenty days later a scaliness was noted along the eyebrow, and in a few days a well marked papular ridge developed. This ridge broke down into an ulcer which discharged serum copiously. Treponemas have been repeatedly found in the serum from this lesion, usually few in numbers, but on one day in abundance. The other eyebrow was inoculated from the first one on January 3, a lesion appeared on February 2. Inoculations have also been made in rabbits' testicles.

The serum from the patient does not give the complement



Papular ridge with ulceration and copious discharge of serum. Incubation, twenty days. *Treponema pertenuis* found repeatedly.

fixation reaction for syphilis. The monkey's serum is also negative in this respect. The patient's blood and urine show nothing noteworthy.

If the infection occurred in the Philippine Islands, the incubation period is eighty-six days, which is very long, although in one of the experimental cases in monkeys the incubation period was ninety-six days; however, it is possible that the rheumatic pains which began about two weeks after leaving the islands were the beginning of a systemic infection which did not break out until late. This is one of the rarer cases of general eruption; all of the yaws are of practically the same age. Beside this case, I have seen one case of yaws in a white soldier who contracted the disease in Balangiga, Samar, where a number of children were affected. He too had a general eruption with several recurrences.

The increase of travel between the Tropics and the United States as a result of our expansion has raised the question of the importation of various diseases, but in the case of most parasites there seems little to fear. A few years ago considerable interest was aroused in England about the possibility of the introduction of *Schistosomum hæmatobium* by discharged soldiers from Egypt and South Africa; but no cases have ever been found arising in England. The possibility of infecting our own Tropics has also come up. In the Philippine Islands I saw a white soldier with a bilharzia colitis contracted in Porto Rico. This man was sent back to San Francisco. In the Philippine Islands I have also seen a Porto Rican and a colored soldier just arrived with *Filaria nocturna*, and *Strongyloides*. *Schistosomum hæmatobium* is unknown in the Philippine Islands, although we do have *Schistosomum japanicum;* the other two parasites are already there.

In the Philippine Islands I have also seen a colored man with ainhum, from Jamaica. It is not rare to have cases of typhoid fever develop on transports going to the islands, and some medical men have claimed that typhoid was introduced into the tropics in recent years, but I doubt this statement as well as the statement that amebic dysentery in the United States is due to imported cases, but this is another story. At any rate, the danger of the spread of yaws seems remote in a fairly clean and well ordered community in the temperate zone.

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[2]Schaudinn & Hoffman: *Arb. a. d. k. Gsndhtsamte*, 1905, xxii, 527; *Deut. Med. Woch.*, 1905, xxxi, 711; *Berl. Klin. Woch.*, 1905, xlii, 673.
[3]Wellman: *Jour. Trop. Med.*, 1905, viii, 345.
[4]Hutchinson: Syphilis. 1909, 4, 8, 35, 544.
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[7]Charlouis: *Vrtljschr. f. Der. u. Syph.*, 1881, viii, 431.
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[9]Ashburn and Craig: *Philippine Jour. Sc.*, 1907, ii, 441.
[10]Prowazek: *Arb. a. d. k. Gsndhtsamte*, 1907, xxvi, 28.
[11]Russell: *Arch. Int. Med.*, 1908, ii, 74.

Discussion.

Dr. Jay F. Schamberg wished to express his indebtedness to Dr. Nichols for the opportunity of seeing this very rare and interesting dermatosis. The chief point of interest would be the differentiation of such cases from syphilis. In the patient demonstrated, the absence of eruption on the trunk with profuse involvement of the face and extremities would argue against syphilis.

Dr. Boleslaw Lapowski referred to the occurrence of syphilitic papules in the folds of skin about the nose and ear, which he considered characteristic of the disease, and asked Dr. Nichols whether he had noticed papules of this kind in yaws. So far as his reading went he had never seen any mention made of papules here. He also asked Dr. Nichols how he could be sure that the spirochete which he had described was the cause of the disease. He thought there was at present no proof that the organism was the etiological factor and that it might be wiser to say only that it was present. The organisms had not yet been satisfactorily described; even Schaudinn had said that he recognized them by instinct, and Dr. Nichols had said that he could not always distinguish the spirochetes of yaws and syphilis. Proof that the spirochete was the cause of syphilis would not be forthcoming until the presence of the organism in an embryo was demonstrated.

Dr. Nichols could not add anything very definite about the localization of the papules in the folds, as had been spoken of. In some cases one found a yaw on the lip which gradually spread up and covered the side of the nose. About the ear he could say nothing from memory. In cases of general eruption, the particular localization did not seem to have much to do with it. In regard to the treponema being the cause of yaws, Dr. Nichols had simply expressed the opinion that yaws was due to a spirochete as certainly as syphilis was.

A CASE OF DELHI BOIL.

JAMES EWING, M.D.

The case which I have to present occurred in the Cornell Dispensary in the class of Dr. James C. Johnston. The patient was a Sicilian, twenty-one years of age, who had been in this country for four years. Three years ago he fell downstairs and hit his forehead on a step, and some time thereafter noticed a small lump or swelling in the skin, which has persisted until now. At the time of examination, this induration in the skin extended over an area about 2 cm. broad, and on palpation the tissues were found to be thickened to a depth of about 0.5 cm. The epithelium was slightly eroded over this area, which was light-colored, and might be described as a large maculo-papule. There was no ulceration. The elevation was about 0.3 cm. at the highest point, and was irregular. The border was also more or less irregular. The consistence was distinctly less than that of a chancre; otherwise it had somewhat the same appearance. The lesion was evidently of considerable dermatological interest, and as the diagnosis was not clear a small piece of tissue was excised by Dr. Johnston for microscopical examination. As a matter of routine many pieces of tissue from various cases in the dispensary practice are examined in the laboratory, and when a section from this lesion came under my eye I hesitated whether to call it infectious granuloma of unknown origin or an endothelioma because of the large number of endothelioid cells. The large cells, however, showed peculiar granulations; and on examination with the oil immersion lens, bodies were found which proved to be the parasites of Delhi boil. There was an infiltration beneath the epithelium consisting of large vacuolated clear cells with pale staining nuclei and minute sharp granules which varied greatly in number. There was no infiltration about the blood vessels and no necrosis; but there was evident degeneration of the phagocytic cells. Minute study of the sections failed to reveal anything of particular histological interest, except to confirm the original impression that the disease was Delhi boil. The most successful staining was done by the old-fashioned Nocht-Romanowsky method. On account of some successful cultivations obtained by Nicolle[1] of such parasites, an attempt was made to secure cultures from this case, and an incision was made through the skin, and the blood and fluid were squeezed out and transferred to several tubes of Nicolle's medium. This medium consists of agar 14.0, sea salt 6.0, water 900, to which is added one-third volume of defibrinated rabbit blood. On this medium Nicolle, as well as Rach and Zarfl[2], secured luxuriant cultures. No satisfactory growth was obtained in this case, however, and a positive result cannot be reported. The morphology of the bodies in the cells, however, seems to be identical with those in the case of Delhi boil reported by Wright, and

[1] *Centralbl. f. Bakteriol.*, 1906, xlii, 488.

[2] *Deutsch. Arch. f. klin. Med.*, 1909, xcvi, 387.

also with the case of kala-azar reported by Marchand, material from which was given to me by Marchand in Leipzig some years ago. I am not prepared to place this lesion in its dermatological series, nor to say that it is a true Delhi boil. It is an infection of the skin showing bodies which are practically identical in appearance with those of kala-azar, and are also identical in appearance with the bodies described by Wright. Possibly they are a little smaller than the bodies seen in either of these cases.

It is interesting to note that this man was in this country for two years before any sign of trouble occurred in the skin; and that the lesion has progressed for two years since the trauma, the relation of which to the lesion is of course very doubtful. No parasites could be found in the blood; the spleen was not enlarged; and there were no signs of any other lesion in the body.

"GRAIN ITCH," A NEW DISEASE IN THIS COUNTRY.

JAY F. SCHAMBERG, M.D.

In the late spring of 1901, there appeared in Philadelphia and its vicinity an unfamiliar eruptive disease which attracted the interest and attention of dermatologists. It was recognized that the disease was new. At that time, having observed a dozen or more cases and photographed several, Dr. Schamberg published a description of the affection in the *Philadelphia Medical Journal* of July 6. Since 1901, this same affection has appeared in greater or less degree from the month of May to the month of October, in Philadelphia and its vicinity. In 1909, at about the same season, an unusual prevalence of this disease was noticed, and an outbreak occurring among sailors on a private yacht lying in the Delaware River attracted the attention of the city and Federal health authorities. Dr. Joseph Goldberger was delegated by the Surgeon-General of the Public Health and Marine Hospital Service to investigate the outbreak. As Dr.

Schamberg had had some experience with the previous epidemics, and was studying the prevailing one, he and Dr. Goldberger conducted the inquiry jointly.

Upon investigation it was found that there had recently been received on this particular yacht a consignment of new straw mattresses, and that only those sailors who had slept on these new mattresses contracted the disease. It was also learned that other outbreaks had occurred on several other boats lying along the river, and on investigation the same conditions as to the receipt and use of these straw mattresses were found. Information was received from various sources and some seventy cases were investigated in the city of Philadelphia occurring in various residences and boarding houses. In every instance it was possible to connect the appearance of the eruption with the use of a new straw mattress. Several of these mattresses were secured, and Dr. Goldberger placed his bare arm and shoulder in contact with the straw for one hour. At the end of sixteen hours the characteristic eruption developed on the arm, shoulder and chest. The straw from the mattresses was then sifted through a very fine sieve, and on careful examination it was possible to detect slight motion. The moving particles were transferred to a slide and microscopically proved to be minute mites, scarcely visible to the naked eye, though the motion was visible. These specimens were submitted to Mr. Nathan Banks of the Department of Agriculture, who identified them as allied to or identical with *Pediculoides ventricosus.*

Dr. Goldberger then applied some of the siftings in a Petri dish to the axilla of a volunteer, and produced the lesions in a short time. Chloroformized siftings, however, failed to evoke the development of an eruption.

All of the mattresses were traced to four manufacturers, and it was found that the one common source of the infected supply was Salem County, New Jersey; one of the manufacturers securing all of his straw from this place.

The lesion produced by this mite was quite characteristic and differed from lesions of other diseases. With the onset of the disease, there is apt to be some constitutional disturbance. Some patients develop fever of 100° to 102°F., with the usual febrile accompaniments. There is sometimes enlargement of the glands, and occasionally chilliness, nausea, and even vomiting may occur. The characteristic lesion of the disease is a hive-like efflorescence on the skin, in the middle of which there is a minute vesicle, extremely small, often only 0.5 mm. in diameter, sometimes 2 or 3 mm. The vesicle rapidly becomes pustular. As a result of the intense itching, the patient scratches the skin and the vesicles are converted into small blood crusts. The eruption is usually extensive and involves chiefly the trunk and extremities, seldom, however, extending below the elbows or knees; the hands and feet are practically always free. The face may show scant lesions. The lesions vary greatly in size, are of a warm rose tint, and slightly raised. The intense itching which is usually present leads to scratching, and the latter to the appearance of excoriations and at times pyogenic complications. One of the patients was suspected of having smallpox, although a greater resemblance to chickenpox is usually presented. In some instances the lesions are much larger than in others; there appears to be an inverse proportion between the number of lesions and their individual size. In some cases, the disease is apt to be confounded with hives, and in others with common "itch"; the absence of the eruption on the hands, and the character of the lesion, would help to eliminate scabies.

Blood examinations were made on the twenty sailors interned at St. Agnes' Hospital; these showed a moderate leucocytosis, the average number in the twenty cases being about 8,500, although some cases had 10,000 and 11,000. Four days later examination showed an average decrease of about 1,000. The eosinophiles at the first examination averaged 5 per cent.; though some patients had 9 or 10 per cent. Four days later the average was reduced to 2.5 per cent. No special cells were found, and the other blood elements were normal. Careful urinary examinations were made, and of the twenty patients, three showed albuminuria; this is doubtless analogous with the albuminuria found in scabies.

The cause being known, the disease was readily cured. Before the cause was discovered, the disease persisted for weeks because the patients continued to sleep on the infected mattresses.

While it was at first thought that the disease was localized to Philadelphia, evidence was later obtained showing that it was much more widespread. In both Indiana and Ohio it has occurred to a considerable extent for the past few years. Farmers gathering straw have been so badly affected that they and their employees have refused to go near the infected straw. In Pittsburg, in 1898, some porters who had carried sacks of barley from a car to a wagon were all badly attacked, and the horses themselves were affected. Dr. Rawles has recently published a series of cases in which farmers and others were attacked in small towns in Indiana. In the August number of the *British Dermatological Journal*, Dr. Willis of Bristol reported an outbreak of an identical disease among some twenty porters who had carried sacks of barley. He made a careful study, but erroneously came to the conclusion that the urticaria was due to vegetable hairs.

The parasite is not new. It was first mentioned by Newport in 1850, and in 1878 was given the name *Pediculoides ventricosus*. A number of outbreaks of an eruptive disease in Hungary and Russia are recorded occurring as long ago as 1849, resulting from contact with wheat and barley. At that time a parasite allied to or identical with *Pediculoides ventricosus* was found.

Microscopical examination of the lesion shows that pathologically it is distinctly an urticaria. One sees an epidermal vesiculation with destruction of the epithelial cells. In the corium there is dense infiltration of round cells and of polymorphonuclear leucocytes. Large numbers of mast cells are present. There is no vertical cleavage of the epidermis to indicate that a puncture has taken place. The parasite evidently does not burrow into the skin.

The mite is predatory and parasitic on soft bodied insects. It has been found on the larvæ of wasps; Prof. F. M. Webster, of the Agricultural Department, has for a number of years been interested in this mite, because it is predatory on the grain-destroying insects. *Pediculoides ventricosus* is of a straw color, long oval shape, with mandibles which act as lancets or needles; the legs are quite characteristic. The mite in the nymph stage has only three sets of legs; later it acquires a fourth pair. When gravid, the abdomen of the parasite swells to an enormous size, twenty to one hundred times the rest of the body.

As has been said, this small mite is of considerable economic importance since the wheat-straw worm, on which it is parasitic, is the great enemy of wheat in the fields of the West, and occasions great havoc. East of the Mississippi, an allied species, the joint worm, does equal damage. In addition to these two grain-destroying parasites, the pediculoides preys upon the grain moth, which attacks the wheat in the barn.

Pediculoides ventricosus finds its nourishment in the larvæ of these insects and destroys them, thus conserving the crops.

In all probability we may look forward to an increasing prevalence of this disease. It appears to be spreading; recently outbreaks have been reported in Italy. No name had hitherto been applied to the disease, and it seemed to Dr. Schamberg wise to give it some designation. He had thought that the name "Grain Itch" would be suitable as a popular appellation and "Acaro-Dermatitis Urticarioides" as a scientific one.

Discussion.

Dr. John A. Fordyce thought that the Society was to be congratulated on the opportunity of listening to this very carefully worked up presentation. It was not often that one had the good fortune to describe a new disease. It had occurred to him that some of the cases described as urticaria in immigrants by Dr. J. C. White several years ago might be the same disease. These cases occurred in newly arrived immigrants in this country, who quite possibly had been infected on the steamer coming over. Dr. Fordyce had seen a number of such cases himself, which were classed as urticarias due to change of diet or possibly as psychical in nature.

DR. BOLESLAW LAPOWSKI asked Dr. Schamberg whether he would be able without seeing the parasite under the microscope to make a diagnosis. Would a person not familiar with the disease be able to make a differential diagnosis between this new disease and other urticarias? Could Dr. Schamberg tell why certain straw was infected, while other straw was not?

DR. SCHAMBERG said that he surmised that Dr. Fordyce's thought was probably correct; some of the cases described as "immigrant itch" probably were cases of this character. He had seen a number of such cases in past years and the resemblance was suggestive. The eruption here, he thought, to anyone who had once seen a well developed case, was absolutely characteristic, provided it was seen before scratching. There was an extensive eruption of an urticarial nature, but most of the wheals were surmounted by a minute vesicle. Unless the source of the infection were destroyed, this eruption continued for a long period of time: it did not run the short course of the usual urticaria. It sometimes might be confounded with the itch, but the absence of lesions on the hands would readily distinguish it. The straw that contains these grain-destroying parasites offers a nidus for the mite also. The United States Government had devoted considerable research to methods of prevention of infection of straw by these grain-destroying parasites. One of the best methods is that of rotation of crops, since the crop of one year is apt to become infected by that of the preceding year.

THE TRACHOMA BODIES IN SMEAR AND SECTION, WITH DEMONSTRATIONS.*

HIDEYO NOGUCHI, M.D., AND MARTIN COHEN, M.D.

PART I.—*Microscopical Studies.* (*Dr. Noguchi.*)

Interest in the question of the etiology of trachoma was suddenly aroused following the announcement of Halberstaedter and v. Prowazek[1] of their discovery of characteristic inclusions in the conjunctival epithelia of a Javanese youth suffering from trachoma. They found these cell inclusions in the smears stained with the Giemsa solution. The original descriptions of the finding may be quoted here.

"Die blauen amorphen Massen der Einschlüsse besitzen dieselbe Avidität zu der blauen Komponente des Giemsafarbstoffes wie die Nukleolen und sind wahrscheinlich mit dem Plastin identisch. Dagegen sind die scharf umschriebenen, distinkt rot gefärbten Körnchen, die schätzungsweise eine Grösse von ¼ μ besitzen, die Träger dieses Virus selbst."

In support of their view of the parasitic nature of these minute granules they report successful transmission of the cell inclusions on some orang-utangs. In the inoculated monkeys they failed to reproduce the typical appearance of trachoma comparable to the symptoms in man. The descriptions of the microscopical examinations of the conjunctival epithelia of the infected apes are so interesting and precise that I do not hesitate to reproduce them below.

"In den nach Giemsa gefärbten Präparaten waren innerhalb der Epithelzellen neben dem Kern in dem licht blauen Protoplasma dunkelblau färbbare, nicht homogene, unregelmässige Einschlüsse sichtbar. Die zunächst kleinen runden oder ovalen Einlagerungen werden allmählich grosser, nehmen eine maulbeerförmige Gestalt an und erfahren eine mit fortschreitenden Wachstum zunehmende Auflöckerung, die im Zentrum beginnt

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*From the Laboratories of the Rockefeller Institute for Medical Research.

In der Folge sitzen sie meist kappenförmig dem Kern auf. Sodann tauchen innerhalf dieser Einschlüsse rot färbbare, distinkte, sehr feine Körnchen auf die sich rapid vermehren, die blau gefärbte Masse verdrängen und allmählich zum Verschwinden bringen. Schliesslich nehmen sie den grössten Teil des Protoplasmas ein, während die blau gefärbten Substanzen nur noch als kleine Inseln zwischen ihnen nachweisbar sind."

The above inclusions disappeared after a week and sometimes they recurred many days later.

Closely following Halberstaedter and v. Prowazek, Greeff[2] published the results of his investigations which had been carried on in Germany for many years. Greeff's descriptions of his trachoma bodies or granules are also most excellent and I wish to quote them here:

"Es handelt sich um sehr regelmässige rundliche Gebilde, die erheblich kleiner sind als die kleinste Coccen. Sie färben intensiv, bald mehr rötlich, bald mehr violett nach Giemsa, schwächer mit Anilinfarben, gar nicht nach Gram. Sie sind von einem, deutlichen, hellen Hof umgeben. Mit stärkster Vergrösserung sieht man zuweilen recht deutlich, dass sie nicht drehrund sind, sondern etwas oval, wie Bakterien mit abgerundeten Ecken. Sie verraten die Neigung, sich zu zwei aneinander zu legen, wie Doppelcoccen. In späteren Stadien liegen sie in grösseren Massen bei einander, meist intracellular in der sogenannten Hufeisenform."

Prowazek proposed to call the cell inclusion *"chlamydozoa"* because of the presence of amorphous masses in a sort of mantle in relation to the minute granules, the real parasites. It may appear somewhat strange that Greeff does not mention the homogeneous mass, but I have seen many instances in which the trachoma granules exist without being accompanied by this substance, and Greeff was not wrong in his descriptions just referred to, and both v. Prowazek and Greeff were dealing with the same parasitic granules. I shall come back to this point when describing our own observations.

Valuable contributions to our knowledge of the trachoma granules have been made by further studies of Greeff, Frosch and Clausen[3], Mijaschita[4], Herford[5], Clausen[6], Greeff[7], di Santo[8], Bertarelli and Cecchetto[9], Cecchetto[10], Leber[11], Grüter[12], Leber and Hartman[13], Lindner[14], v. Prowazek and Halberstaedter[15], Heymann[16], Krüdener[17], Stanculeanu[18], Wolfrum[19], and others. Brown Pusey[20] and Verhoff[21], in America, have each reported a case of trachoma with the trachoma bodies. Except some cases of blenorrhea with and without gonococci the trachoma bodies have not been found in any other condition outside of trachoma. All investigators agree on one point, namely, the difficulty in finding the trachoma bodies in treated cases. Even in comparatively fresh and untreated cases, one may not find more than one after several hours' search through several smear preparations. In some cases they are extremely scanty, while in a few cases they may be found in every preparation.

The trachoma bodies have been found in sections by di Santo[22], Wolfrum[23], Radziejewski[24], Herzog[25], Lindner[14], and others.

Stargardt first reported a similar cell inclusion in a case of gonorrheal blenorrhea of a new born child. This finding was followed by the communications of Halberstaedter and Prowazek, and Lindner, who found the chlamydozoa in the epithelia of the conjunctiva of several cases of blenorrhea neonatorum non-gonorrhœica. Heymann also reports the chlamydozoa finding in some cases of gonorrheal conjunctivitis. Römer[26] obtained negative results in his examination of one hundred and four cases of trachoma, while Heymann was unable to find the inclusions in five out of ten untreated fresh cases of the same affection.

Our Own Observations:—With the clinical co-operation of Dr. Cohen I have been able so far to examine about three hundred cases of eye affections, including trachoma, gonorrheal conjunctivitis of new born and adults, non-gonorrheal blenorrhea, simple conjunctivitis, chronic conjunctivitis, vernal catarrh and various other forms of bacterial conjunctivitis. A large number of normal conjunctivæ of man (fifteen persons) and animals (monkeys, rabbits, cats, dogs, sheep, goats, hens, guinea-pigs) have been examined as controls. The work in the direction of animal experiments is now in progress, and the results will be our next subject of communication.

Before presenting the results of our examinations I wish to describe briefly the technique which I found most useful for the search of the trachoma bodies.

Smears:—I employed Giemsa stain (Grübler*) twenty-four hours after which time the slides with smears are quickly decolorized in the following manner: Dip in aceton for five to ten seconds; transfer to distilled water. If overstained put in a 10 per cent. solution of glycerinethermischung (Grübler) for one or two minutes. Wash in running water for a few minutes. Blot and dry in the air. One may examine with cedar oil directly, or the smears may be mounted with cedar oil. Trachoma granules stain intensely bluish-violet, the "plastin mass" more bluish; nuclei, bright reddish-violet; protoplasm, pale bluish; mast cell granules, reddish to reddish-violet; red corpuscles, eosin color.

Sections:—Tissues are fixed in sublimate alcohol as recommended by Giemsa[27] in his recent moist method of applying his stain to smears. After twenty-four to forty-eight hours of staining the tissues pass through graduated alcohol, etc., to paraffin embedding and sectioning. Before staining the sections are treated with alcoholic iodine solution, washed in water, treated in a 0.5% solution of sodium thiosulphate, and washed in water. The sections are then stained with freshly prepared solution of Giemsa fluid (10 drops to every 10 cc. of water) with an addition of one drop of 1 per cent. potassium carbonate solution to every ten cubic centimeters of the dilution. After twenty-four hours, the slides are placed in 10 per cent. solution of glycerinethermischung (Grübler) for about five to ten minutes. The sections become distinctly reddish by this treatment. Wash the sections in water for about eight to ten minutes. Transfer the slides to aceton, aceton 70+xylol 30, aceton 50+xylol 50, aceton 30+xylol 70, and xylol, and mount in cedar oil.

*Ten drops of the stain and one drop of 1 per cent. potassium carbonate solution to every 10 c. c.

I found that by the above method the trachoma granules may easily be differentiated from certain other granules which otherwise may be mistaken for the former on account of minute size and violet-staining property. This confusion which sometimes occurs in the interior of the tissue, where there may be found scattered granules of mast cells, is eliminated by the differentiation just described, for the trachoma granules remain bluish-violet, while the mast cell granules become reddish-purple. The more highly differentiated, the more bluish the former and the more reddish the latter become. In sections the nuclei of the epithelial cells may fail to stain in the usual reddish-violet color as in the smears, and in this case they become rather pale-blue after differentiation. Zenker-fixed tissues show this tendency. In properly differentiated sections the contrast of the trachoma bodies and other granules is most striking.

Unna's polychrome methylene blue and glycerinethermischung method for mast cells also gives a satisfactory contrast stain in which the trachoma granules as well as initial granules are bluish, the mast cell granules are reddish, erythrocytes pale-red, and nuclei bluish.

Other stains were not as satisfactory as the above methods.

Results.

Our findings may be tabulated as follows:

Diagnosis.		*Trachoma Bodies Found.*	
		In Smear.	In Section.
Trachoma—			
Follicular type	180	1	1
Acute and Hypertrophic types	60[1]	20	16[2]
Blenorrhea—			
Gonococcal	15	0	—
Non-gonococcal	10	0	—
Vernal catarrh	4	0	—
Acute conjunctivitis	15	0	—
Chronic conjunctivitis	15	0	—
Normal conjunctiva	15	0	—
	314	21	17

Remarks on the Trachoma Granules.

Smears:—The trachoma granules are principally found in the cytoplasm of epithelial cells. In a great many cells the granules group themselves in the form of a crescent or half-moon conforming with the convexity of the nucleus and almost always in direct contact with the latter. There are sometimes roundish or oval shapes as well. The size of these heaps of granules (so-called trachoma bodies), which stain rather intensely bluish-violet by Giemsa, is very variable. Some are as large as the nucleus, some very minute. On the other hand, the entire epithelial cell may be filled up with one enormously extended mass of granules. An epithelial cell may contain more than one such grouped granular mass. There are two distinct varieties of granules in a moderately large heap, one minute and one coarse. The coarse granules lie usually along the periphery, while the finer granules are within the interior. The coarse granules seem to stain more bluish, and often assume the appearance of an irregular, less intensely stainable, apparently homogeneous mass, the so-called plastin rest of Halberstaedter and Prowazek. On the other hand, the minute granules seem more uniform in size and measure, about 0.25 μ there being sometimes two together like a diplococcus. The trachoma bodies of smaller sizes are somewhat different in composition. They usually contain more of the coarse granules than of the minute sort. In some bodies the former alone are recognizable, in which the bodies appear like small rosettes stained distinctly more bluish than the advanced stage of development of the same. On the

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[1] For forty-five cases reported, we are under deep obligation to Dr. Stormer, Ellis Island Hospital, New York, and we express our thanks to him and to Dr. Guthrie, Dr. Dunn, and other officers for their ready assistance in getting suitable cases. Out of forty-five cases five were positive.

[2] These sixteen cases are among the twenty positive smear findings; the remaining four cases could not be examined histologically.

other hand, there are some epithelial cells which are filled with the minute type of granules. Here the number of granules may be enormous or they may be rather sparse. The bluish staining coarse granules at the periphery are not so numerous or often not found. The cells appear distended and the thin wall which is almost unrecognizable is sometimes seen to have ruptured with the minute granules escaping around the infected epithelia. Very frequently one sees a clear vacuolated space surrounding the trachoma bodies. While studying different cases I was struck with the fact that in certain cases this vacuolization is more pronounced than in other cases. It was also noticed that the presence of the coarse granules and their number are more abundant in certain cases. Thus, I sometimes found a mere heap of uniform granules of smaller type in the cytoplasm without being associated with bluish coarse granules. The number of such granules may be only one or two, or they may be innumerable. This suggests that the epithelia in this case react somewhat differently from those in which the coarse granules predominate. In the latter instance the invasion of the trachoma-granule is easily indicated with the presence of the coarse granules in the infected cells.

Free trachoma granules in smears have been seen only around the epithelia bursting with the granules, and I cannot say that the detection of these free granules is an easy matter.

Sections:—Stained by the method I described, the trachoma granules can be readily traced in the sections. By the Giemsa-plus-glycerinether mixture method, the granules are bluish-violet in color, while other granules that may confuse the differentiation by morphology alone will become reddish. By Unna's mast cell stain the trachoma granules appear bluish and the mast cell granules bright reddish. The nuclei are rather pale bluish. The red corpuscles are pale reddish-yellow. Contrary to what is true of smear preparations, the trachoma bodies in sections seem always to be composed of the two varieties of granules, as has been the case with certain smear preparations. The coarse granules, which take the bluish stain more intensely than the minute kind, are situated along the periphery of the trachoma granule heap (bodies). The inner minute granules stain less bluish, but more violet with the Giemsa, and weakly bluish with the Unna method. In the early stage of development these bodies are very small, only the size of a gonococcus, and may be found scattered in a cell. In this stage the minute granules are not easily seen.

The surface layer of epithelium of the infected conjunctiva is the *usual* seat of location of the trachoma bodies. In certain regions practically every cell is infected and varying stages of development of these parasites may be found in one field. Multiple infection of an epithelial cell is very common. In a case of advanced trachoma with follicular conjunctivitis (patient Haber) I found that in the subepithelial layer where abundant small cell infiltration and active macrophagocytosis were present, there were some cells infected with the trachoma bodies of different developmental stages. These trachoma bodies were readily distinguished from any other granules by the methods I have here described. I was unable to find any trachoma bodies or free trachoma granules in the interstitial connective tissue. I have once encountered trachoma granules in a leucocyte (?) and in an endothelial cell in the follicle.

By studying a series of smears and tissues from some cases, I found that it is difficult to predict the number of trachoma bodies in tissues from the number of the bodies found in the smears. Very often I obtained a good section from a case in which smears were scanty in the bodies, and vice versa.

It is our custom to examine about four slides from each case. I often found only a single epithelial cell with trachoma bodies after a careful search of several slides. It is a most tedious undertaking, and a single microscopical examination may fail to reveal the presence of the trachoma bodies in a positive case.

PART II.—*Clinical Studies.* (*Dr. Cohen.*)

Regarding the clinical appearance of the cases studied by Dr.

Noguchi, in which the Prowazek bodies were found in smears and sections, the following classification might be considered:

I. Follicular type.
II. Acute type.
III. Hypertrophic type.

I. In the follicular type, the following condition prevails: few or numerous follicles, soft or hard (majority soft), cover a part or the entire conjunctiva—the cornea and the appendages are not involved.

There are no acute manifestations present, and the individual is unaware of any eye affection until a conjunctival examination reveals the condition.

Of this type numerous examinations were made, but the Prowazek bodies were found in only one case, that of a boy (Haber) fourteen years of age, born in this city of Austrian parents.

His conjunctiva was expressed under a general anesthetic a year ago. He received after treatment consisting of copper sulphate stick applications for two months. Treatment then ceased for ten months, when, on account of relapse or recurrence, the conjunctiva was again expressed, and the smear and section showed the Prowazek bodies.

The mother's conjunctiva was studded with numerous soft follicles in the lower lid, and a few in the upper lid, but no Prowazek bodies were found in her case.

II. Acute type.—In this group the following symptoms were present: The lids slightly swollen; profuse serous secretion with slight pain and photophobia; intense conjunctival congestion; follicles present in the lower lid and in the retrotarsal fold; commencing infiltration in the superior part of the cornea. As a rule the Prowazek bodies were found in this group of cases.

III. Hypertrophic type.—The symptoms of which are as follows: Lids thickened; slight serous discharge; occasionally pannus, entire conjunctiva thickened and congested; usually a few hard follicles are scattered in upper and lower lid; in this division the Prowazek bodies have been found less frequently.

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Discussion.

DR. J. E. WEEKS said that the demonstration of these trachoma bodies was made in this country some two years ago, though not, he believed, in either New York or Philadelphia. Recently they had worked on the subject at the New York Eye and Ear Infirmary, and the bodies had been obtained, but only, he believed, in smears from fresh cases. Lindner of Vienna had demonstrated their presence in old cases as well. Familiarity with the technique would, Dr. Weeks believed, enable us to find these bodies in a very large percentage of cases of trachoma. As Dr. Noguchi had said, they had also been found in cases of ophthalmia neonatorum which were not gonorrheal. Dr. Weeks had recently received some very beautiful drawings from Dr. Lindner of Vienna, showing the trachoma bodies in various stages, and the same bodies in the secretion of ophthalmia neonatorum. The parasite had been obtained from the conjunctiva of a monkey inoculated from the vagina of a woman whose child had the infection. While it was probable that the parasite was the cause of trachoma, Dr. Weeks did not think that it was generally accepted as such yet. Further studies must be made before this point was determined. The infectious nature of the organism, however, had been demonstrated by inoculations from trachomatous conjunctivas to the conjunctivas of the higher monkeys, as Dr. Noguchi had said. The organism had also been recovered from the eyes of monkeys which had been inoculated with trachoma from human beings.

A CASE OF HEMORRHAGIC APOPLEXY OF THE PANCREAS.

JOHN H. LARKIN, M.D.

Dr. John H. Larkin presented a specimen of hemorrhagic apoplexy of the pancreas. The patient was a man of twenty-eight years, a gambler and man about town, who presented himself at the hospital two months before, complaining of severe pain, collapse, and vomiting. He was received into the hospital, where he went into a partially comatose condition after four or five hours. The following morning the symptoms were almost all cleared up. During his four days' stay in the hospital he had attacks of collapse which were rather profound, accompanied by very low pulse and an increased amount of albumin in the urine. There was also pain and intermittent vomiting, accompanied by some blood. He remained well from the time he left the hospital until he was taken back two days before, in the same condition. He was in extreme collapse and had a good deal of pain, especially in the epigastric region. After six or eight hours, he went into coma, and died.

At autopsy a rather peculiar condition was found when the abdomen was opened. At the pyloric end of the stomach what was at first thought to be a tumor was seen, but on further investigation it was shown that there was no tumor, but that bulging into the duodenum there was an elastic fluctuating mass which somewhat narrowed the tube. On dissecting back of the stomach the condition of hemorrhagic apoplexy of the head of the pancreas was found. The fresh clot of blood was still in position. A probe could be passed with some freedom into the upper portion of the head of the pancreas. In this area there was a fresh clot. In dissecting the large blood vessels and tracing the splenic artery, no occlusion nor lesion of the wall of the artery could be found; but on going down to the hepatic artery, and from there down, there was a marked difference of caliber, and no communication could be found from this artery into the head of the pancreas. The pancreas was very hard, elastic, and fibrous. The question arose, what had happened to this patient two months ago? At that time a large mass was felt on the left side and a tentative diagnosis of hydronephrosis was made. At the autopsy a peculiar cystic mass was found at the tail of the pancreas. Whether that mass was simply a cyst of the tail of the pancreas, or whether it was a mass which two months ago represented a hemorrhage which had become absorbed was a question.

THE EFFECTS OF SYPHILIS IN THE MENINGES.

CHARLES B. DUNLAP, M.D.

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I.

I wish, in discussing the changes which syphilis may produce in the meninges of the brain and spinal cord, to present in addition to the gummatous type, a form of meningitis of syphilitic origin which, as far as I am aware, has received little attention. It may be found briefly described among the varieties mentioned by Alzheimer in 1904, but is only casually mentioned in the literature.

Cerebral syphilis is regarded by many general pathologists as a rather rare disease. We have not found it so if we include in cerebral syphilis the effects produced by this disorder in the meninges and in the vascular apparatus. The role which syphilis plays in insane hospitals may be judged from the fact that in a material of one hundred and twelve brains received in the past year, from the State hospitals for the insane, twenty showed evidence of syphilis in the meninges, the vessels, or both; and none of these twenty cases were of the gummatous type. In this same material of one hundred and twelve brains, there were twenty-three cases of general paralysis, and twenty-seven of ordinary arteriosclerosis. This proportion of syphilitic cases (18%) is higher than would be found in the ordinary autopsy service of a State hospital. The hospitals seldom send brains from cases of manic-depressive insanity, dementia præcox, etc., to the Institute, but the cases which they do send are picked out on account of some specially interesting features. In the last one hundred autopsies at the Manhattan State Hospital (which would be fairly representative) I have not the exact number, but Dr. Rusk, the pathologist, was able to recall, without looking over the autopsy records, five of cerebral syphilis.

II.

Gummatous Form:

In the nodose or *gummatous forms* of cerebral syphilis, one may find in the meninges separate nodes of variable size presenting necrotic centers surrounded by a zone of lymphoid and plasma cells, and still more externally by more or less connective tissue; or the nodes may be of smaller size and near enough together to become confluent; or they may be of miliary size, as in a case to be shown later. With these gummatous varieties, a diffuse meningitis, or a more patchy meningitis may be associated, or (more rarely in my experience) the meninges may be essentially clear except in the close neighborhood of these nodes. The latter are situated, as a rule, in the meninges (seldom in the brain substance) and the inflammatory process is prone to invade the neighboring brain tissue both by direct extension, and by way of the vessel sheaths. In the Institute collection of over five hundred brains, we have ten examples of this gummatous type of syphilitic meningitis.

III.

The Diffuse or Non-Gummatous Form:

This diffuse type, which is more especially dealt with in this paper, consists in either a diffuse or a patchy meningeal exudate composed of lymphoid cells and a variable but usually a smaller number of plasma cells; gummatous nodes are absent. There is nothing characteristic in the cellular make-up of this exudate; it seldom contains polynuclear leucocytes, and endothelioid or phagocytic cells are relatively few. Sometimes it is most abundant on the basal surface of the brain, especially in the interpeduncular space and about the optic nerves, sometimes it is quite as abundant on the convexity. In the latter position, it will often be found in the depths of the fissures or in the neighborhood of blood vessels, especially in the loose adventitial sheaths of the latter, and in places where the exudate is massive and the process more intense, all layers of the vessels may be penetrated by the exudate. One seldom finds a diffusely spread, abundant exudate, such as is seen in the more acute types of meningitis. Large stretches of the pia may look perfectly clear or show only fibrous thickening, and on gross examination the pia may vary little from the normal, but, on the other hand, it may be much thickened and show considerable opacity; granulations of the ependyma are usually present. There is no invasion of the brain cortex by the exudate except that occasional lymphoid cells and sometimes a few plasma cells may be found in the sheaths of these blood vessels, which enter the cortex through the meningeal exudate; these are plainly extensions of the meningeal exudate along the vessel sheaths. Often the exudate is most abundant in the pia of the brain-stem, the medulla oblongata, and the spinal cord, and in these positions it seems more prone to extend by way of the vessel sheaths into the interior.

Along with this diffuse or patchy meningeal infiltration is to be found, in the majority of cases, a girdling endarteritis of the Heubner type, the intimal tissue being firm, usually organized and laid down in concentric layers. This process in the vessels is for the most part not general, only a few vessels may show it, and those are frequently the larger branches, such as the trunks or the main branches of the Sylvian arteries, or the basilar artery. The more carefully it is looked for, the more frequently it will be found.

To summarize this form of meningitis:—it consists of either a diffuse, or, more often, a patchy interrupted exudate composed chiefly of lymphoid and plasma cells found in the meninges of the brain, brain-stem and spinal cord, and in the sheaths of the blood vessels, the walls of which it frequently penetrates: associated with it is usually an endarteritis of the Heubner type, but the arterial lesions may be confined to a relatively small number of vessels, and may be found only after prolonged search.

IV.

Differentiation:

Under this heading I shall attempt to differentiate only the diffuse or non-gummatous form, from those conditions which may resemble it.

General paralysis presents the same cellular elements in the pia, but in addition to the pial inflammation there is always a diffuse inflammatory process in the cortex and subcortex characterized by infiltration of the vascular sheaths with lymphoid and plasma cells; this general infiltration of the cortical vessels is not dependent on that of the meninges, nor is it an extension from them; it may be excessive where the meningeal infiltration is slight, in other words, there is no relation between the two; in the syphilitic forms of meningitis, on the other hand, if the cortex is invaded at all the direct relation of this invasion to the meninges is plain.

Tuberculous meningitis, especially if chronic, both in distribution and in the character of the exudate, may closely resemble the diffuse syphilitic form, but there are certain differences (aside from the presence of the tubercle bacillus) which are usually readily demonstrable in tuberculous meningitis. In the material at my disposal there is less tendency in the tuberculous process to invade the cortex and neighboring tissues, and a greater tendency to degenerative changes, the tuberculous tissue being less organized and less vascular. The cellular exudate itself contains, in tuberculous meningitis, a larger proportion of leucocytes and endothelioid cells, whereas in the syphilitic meningitis these are much in the background. Another decided difference is found in the reaction in the intima of the blood vessels, where, instead of a thick, firm resisting girdling intimal layer, such as is seen in the syphilitic cases, the endothelium in the tuberculous cases is, as a rule, merely raised and carried inwards as the result of a crowding of the subintimal tissues by cells of endothelioid and lymphoid type.

The more acute forms of meningitis would hardly come into question in the differentiation, the character of the exudate being for the most part quite different, not to mention the presence of pathogenic bacteria, and the absence of a characteristic reaction in the blood vessels such as has been described in syphilitic meningitis. The clinical course is also entirely different. In the ordinary forms of arteriosclerosis there is no inflammatory process in the meninges.

V.

Diagnosis:

The diagnosis, on anatomical grounds, of syphilitic meningitis of non-gummatous type, consequently rests upon the presence of a diffuse or patchy cellular exudate in the meshes of the pia, and in the adventitial sheaths of the blood vessels, with, not uncommonly, penetration by the exudate into the other coats of the vessels, and the presence of an endarteritis, considered since the days of Heubner to be of specific type when found in the cerebral blood vessels. This same type of endarteritis is found in the gummatous cases; in these, moreover, there is often a diffuse or patchy meningitis of the kind described above under the diffuse form of syphilitic meningitis.

Whether or not gummata may occur in a given case of syphilitic meningitis depends upon factors which I cannot weigh; but the absence of gummata, I believe, in no way interferes with a positive diagnosis.

Concerning the clinical course of the diffuse meningeal cases I can at present say little; a fair proportion of the patients give a definite history of syphilis at a remote period; others show signs of syphilis, still others deny syphilis. In some the diagnosis of general paralysis had been made clinically, in others that of arteriosclerosis was made. This non-gummatous form of syphilitic meningitis is probably to be looked on, at least in most cases, as a late development, in the so-called tertiary period of syphilis or perhaps even beyond it.

I have not referred to the Wassermann reaction in these cases. It has not been carried out as a rule; neither have the tissues under consideration been examined for *Spirochæta pallida*, except in a case which showed miliary gummata, where it was found by Dr. James Ewing, who was kind enough to examine some of the material. Where lumbar puncture was performed it gave a lymphocytosis as a rule. Much work remains to be done on the group both clinically and anatomically.

The lesions described were illustrated by a series of lantern slides.

A PRELIMINARY REPORT ON THE GENERAL AND SYPHILITIC FORMS OF CEREBRAL ARTERIOSCLEROSIS.

CHARLES I. LAMBERT, M.D.

(Psychiatric Institute, Ward's Island, New York.)

The aim in the study of any disease process is to ascertain in all possible detail the nature of the mechanism underlying the pathological condition. The etiology of general arteriosclerosis offers many difficulties and is only partially understood. Almost everything which is generally considered injurious and in disharmony with the constitution of the individual has been assigned as a cause. We think of heredity, of the individual's constitution, of habits and occupations, of the various intermittent or permanent physical or mental stresses and strains in life, of organic and inorganic poisons, of metabolic disorders, of intercurrent infections and intoxications, and realize that they, individually or severally, combine to favor conditions of arteriosclerosis. To trace their direct relationship, however, is well nigh impossible, largely because cause and demonstrable effect are usually remote from each other in point of time.

The fact that arteriosclerosis may occur spontaneously in the lower animals is of considerable biological interest in relation to the development of human arteriosclerosis. Lyding observed it in cattle, horses, and dogs; while Blair, veterinarian to the Bronx Zoo, reports it as quite common in birds, especially the ostrich and emu.

Experimental medicine has endeavored to foreshorten nature's methods of producing arteriosclerosis. Numerous attempts made to reproduce arteriosclerosis in the lower animals by blood pressure stimulants and depressants such as adrenalin, barium chloride, etc., have not given uniform results which are wholly convincing and comparable to conditions as seen in human arteriosclerosis. These several reagents seem to affect primarily the media, causing degeneration and subsequent calcification of the smooth muscle fibers, together with stretching and fracture of the elastic fibers and secondary thickening of the intima. The increased blood pressure and to a less extent the toxic element have been assigned as the active factors in producing this type of arteriosclerosis.

In addition to the high blood pressure and toxic conditions, there can be little doubt that there are other factors which impair the elasticity and lower the permanent integrity of the arterial wall, notably, the infections and toxemias. The arteriosclerotic lesions thus produced are more comparable with human arteriosclerosis. Wiesel, examining the central and peripheral arteries of persons dying at the climax of acute infections, and again of other persons recovering from acute infections but dying months or years later, found in the early cases degeneration, mainly in the media, and in the later cases evidence of reparative changes.

In connection with these findings it is of importance to compare the relative effect of certain bacteria upon the different tissue components of the vessel walls. The action of certain organisms, *e. g.* streptococcus, pneumococcus, typhoid, etc., on the endocardium is well known; the effect upon the vessels themselves has been less studied. Some organisms seem to involve the entire vessel wall in destruction; this is more particularly true for the strictly pyogenic group of bacteria; the typhoid bacillus and pneumococcus particularly, stimulate endothelial proliferation; the tubercle bacillus, a strong connective tissue reaction, while the *Spirochæta (treponema) pallida* may stimulate any one or all of the mesoblastic tissues to a marked activity. This tendency of certain bacteria to exert a selective action upon the different tissues is of considerable interest, not only with reference to the acute lesions but to the remote effect of such lesions in possibly increasing the vulnerability of the arterial walls in the regressive period of life.

To summarize these observations, the most evident and probable factors operating together in producing general arteriosclerosis may be classed under two main headings, first a relative increase in the strain thrown upon the blood vessel wall by heightened blood pressure, and second, an intrinsic weakness of the vessel walls due to hereditary weakness or defects acquired through disease. The action of normal or heightened blood pressure in widening the lumen of the weakened vessel locally or diffusely, depending upon the extent and distribution of the wall defects, congenital or acquired, and the reaction of the intima in a hypertrophic and hyperplastic manner to repair the defect, is the mechanism which probably underlies the development of the arteriosclerotic process. Following close upon this reparative or compensatory reaction is the essentially regressive stage which complements the vicious circle.

Under general arteriosclerosis we have what might be termed (1) a physiological arteriosclerosis, and (2) the pathological forms of general arteriosclerosis, (a) atheroma or atherosclerosis affecting the larger cerebral vessels, (b) colloid-calcareous degeneration developing most frequently in the smaller, usually medullary vessels, and (c) arteriocapillary fibrosis involving the finer arterioles and capillaries, particularly the cortical vessels.

The term physiological arteriosclerosis is used in a relative sense. The climax of growth is attained usually in the third decade of life. The completion of the normal growth is followed almost immediately by regressive changes. The parenchyma of any organ shows regressive changes relatively earlier than the conjunctival tissues, and these skeletal tissues in part at least may be substituted for the nobler tissue elements as the latter degenerate. These changes occur earlier in some individuals than in others; in all individuals these regressive alterations inevitably lead to some degree of arteriosclerosis which may be physiological and concomitant to old age. On the other hand, vascular thickening becomes pathological when it anticipates in time, degree, and severity the physiological condition of normal senescence. Various grades of general arteriosclerosis may be seen beginning as early as the fourth decade of life, but particularly in the fifth, sixth, and seventh decades.

(a) The gross appearance of general arteriosclerosis, atheroma, as it affects the larger vessels, scarcely needs description. The lesions vary much in their distribution, sometimes affecting the larger trunks, again the medium sized and smaller vessels. If the lesions are wide-spread they are spoken of as arteriosclerosis diffusa, if scattered and localized as arteriosclerosis nodosa.

The atheromatous plaque is first apparent as a thin, gray, translucent flake on the intimal surface, later it becomes harder, of a cartilaginous appearance, and, finally, degenerating becomes yellowish and atheromatous. A transverse section through one of these plaques shows its signet-ring, non-girdling extent. Our knowledge concerning the initial changes is vague. Aside from the possible congenital intrinsic wall defects, the possibility of parenchymatous alterations and intimal reactions referable to injury is not entirely unlikely. Among the earlier changes concerning which we have demonstrable facts are those seen in the elastica and media of the vessel wall; the nuclei of the latter stain palely, and the cell cytoplasm appears cloudy, and the deeper media gradually degenerates. The vessel wall is relatively weakened at this point, dilates even under normal pressure; but in this period of life blood pressure is usually heightened. To repair and compensate for the weakened wall and widened lumen, the more responsive intima proliferates. This new-formed tissue is in no sense inflammatory; it is largely endothelial in type and origin; it has little or no plastic or stable tissue-forming properties, and uninvaded by new-formed vessels is wholly dependent upon the axial blood stream for nutrition. These conditions render the plaque peculiarly susceptible to degeneration, especially in its deeper parts. Added to these factors favoring degeneration of the endothelial plaque is the late period of life in which these changes occur. Biologically speaking, in the later period of life there is a relative weakness of the cells to regenerate themselves and especially to repair damages in a compensatory manner and resist degeneration. This is in contrast with the reaction of cells earlier in life stimulated to proliferation by a powerful irritant as occurs in the progressive, essentially syphilitic, forms of arteriosclerosis. We can, therefore, better understand why, in the later decades of life, the response to reparative changes is weaker, the product less resistant to degeneration and the end result, atheromatous degeneration, somewhat different than in the progressive forms of arteriosclerosis. The atheromatous type of arteriosclerosis affects particularly the larger cerebral vessels and is responsible for the more voluminous cerebral lesions either through softening or hemorrhage, and therefore the grosser forms of defect symptoms as hemiplegias and hemianopsia.

(b) In the colloid-calcareous type of general arteriosclerosis there is an infiltration of the media with a colloid-calcareous material. It appears first as fine granules in the deeper coats of the media, probably intercellularly at first, but with the accumulation of this material the granules become confluent and entirely replace the muscularis which is probably largely destroyed by pressure necrosis. With the substitution of this friable, colloid-calcareous material for the muscular coat, the resisting power of the walls is lowered and the vessel is dilated. To compensate for the widened lumen, the intima proliferates. Colloid-calcareous infiltration of the vessel wall may continue, always occurring centripetally and usually concentrically, finally resulting in obliteration of the vessel with softenings, or sometimes rupture with small hemorrhage. The lesions are naturally small, often multiple and usually isolated, and the defect symptoms correspond.

(c) In the third form of general arteriosclerosis, arterio-capillary fibrosis, the vessel walls are uniformly thickened and composed of an anuclear connective tissue, or of palely staining nuclei in a matrix of homogeneous and finely fibrillar connective tissue. It may involve a terminal arterio-capillary system and produce numerous discrete cortical and subcortical softenings. The anuclear and fibrillar character of the vessel walls, absence of inflammatory infiltrate, lymphoid and plasma cells, the type of softening, the latter usually characterized by an abundance of granule cells, the less evident tendency to a local neuroglia reaction and sclerosis distinguish it from a closely comparable condition due to syphilitic endarteritis of the terminal vessels to be described later. The lesions are discrete, patchy or diffuse. The brunt of the process falls particularly on the nervous parenchyma, and the defect symptoms, instead of being focal, may be irritative or absent; the same is likely to be true of the mental disorder of a diffuse and non-systemic character.

Under the *progressive* forms of arteriosclerosis there is the endarteritis obliterans of Heubner. The essential if not the sole cause of this form of arteriosclerosis is syphilis. Cause and effect stand in such close proximity, or if long removed from each other the specific features in their relationship usually remain so demonstrable that we may trace the life history of the process with considerable precision. The histological features of the various so-called stages of syphilis have many points in common. There is a marked reaction on the part of the mesoblastic tissues focally or diffusely manifesting itself as an infiltration of the fixed tissues with lymphoid, plasma cells and occasional mast cells, and concentric girdling proliferation of the intima of the blood vessels. The focal or diffuse character of these changes as they occur in the brain, presents anatomical and clinical varieties of syphilitic disorders. It is convenient to make three fairly distinct groups of syphilitic brain disorders. (1) The focal or gummatous type, (2) the diffuse meningeal forms, and (3) the endarteritic disorders of the larger and smaller vessels.

(1) The *focal* or *gummatous type:* The clinical complex

may closely simulate brain tumor. (2) Opposed to the focal type, is the *diffuse meningo-encephalitic* process giving rise to a meningeal complex more especially. Intermediate or combination forms of these two types are not uncommon. (3) In contradistinction to these two types, i e., the focal and diffuse, which are frankly inflammatory in nature, there are the *endarteritic* forms in which the inflammatory features are usually less evident and significant, and the tissue alterations have largely to do with the vessels themselves. The clinical features are comparable with those associated with general cerebral arteriosclerotic disorders. It is the endarteritic forms which concern us especially at this time. Two forms of endarteritis may be distinguished, (a) in which the large vessels are chiefly affected, Heubner's type, and (b) in which the small cortical vessels, Nissl's type, are involved.

A detailed study of the cerebral arteries was not made in all the cases of supposed arteriosclerosis received at the Psychiatric Institute for the past year, but in a large number of those examined, eighteen out of forty-eight cases, specific endarteritic and associated changes were found. This probably does not represent the normal ratio of occurrence at autopsy, since the material sent to the Institute consists largely of cases chosen for their clinical or anatomical importance. The histologic changes present in these cases consist of a concentric girdling proliferation of the intima of the vessels together with a more or less marked production of new elastic tissue. The amount of elastic tissue produced depends largely on the chronicity of the process. Accompanying the endarteritic changes there is usually a meso— or peri-arteritis. With this inflammatory reaction there is the development of new vessels which penetrate the new formed intimal tissue providing additional nutrition and making possible organization. The collagen fibrils of the new connective tissue thus formed are substantially resistant in themselves to degeneration and, when finally degenerating, the transformation is rather of a hyaline than a fatty nature in contrast to the fatty degeneration seen in the atheromatous process; however, the latter condition may be superimposed late in life where the individual survives the earlier endarteritic process.

The abundance of the lymphoid and plasma cell infiltrate in the vessel sheaths and pia of the endarteritic process is proportioned very considerably with the activity and age of the process, being most marked in the relatively acute conditions or those of a strikingly episodic development. It does not seem to bear any particular relation to the remoteness of the syphilitic infection but rather to the process itself. Usually, however, in cases of long standing, twelve to fifteen years, only a trace of meningitis and vascular sheath infiltration with lymphoid and plasma cells was demonstrable. This was particularly true in cases of slow development and long standing, fifteen to twenty to twenty-five or thirty-five years, lymphoid and plasma cells, especially the latter, being almost completely lacking, and mast cells in a fair number being found in addition to the endarteritic changes.

The endarteritis affecting the smaller vessels was first referred to by Nissl, but has not been described by him in detail as yet. It is possible and strongly probable that in this disorder we have a special form of syphilitic brain disease before us. It manifests itself by a tremendous endothelial reaction in the finer blood vessels of the pia and cortex especially. The original capillary wall becomes several cells thick, and new capillary sprouts are formed. The cells of the sheath grow extremely rapidly and abundantly and revert to a primitive type, thus the cells of the intima and adventitia may be indistinguishable. The nuclei are rich in chromatin, mitoses are seen, and the cytoplasm of the cell stains deeply. Rod cells are seen in the neighborhood and a relatively acute neuroglia reaction is present; comparatively few gitter and granule cells are found. Discrete or patchy softenings usually result which develop slowly and, because of the marked local neuroglia reaction, terminate rather in the form of a cortical gliosis with sclerosis than as a focal softening with the abundance of granule cells usually seen in the regressive type of arteriosclerotic softening.

The chronic aspect of this cortical blood vessel disorder is more frequently seen than the acute phase. There are several cases in the Institute collection which very probably logically belong here. In these cases there is the history of syphilis, a characteristic endarteritis obliterans less marked in the larger vessels but conspicuously evident in the smaller cortical vessels, associated with which are numerous small softenings or areas of a diffuse cortical sclerosis which is systemic in some cases, almost general in others. The unequal involvement of the vessels, the comparatively large size of the vessel wall cells, the number of collagen fibrils in the cell cytoplasm, the absence of mitotic figures and absence of embryonic cellular features distinguishes it from the acute condition. Clinically these cases often show irritative symptoms and are usually diagnosed epilepsy, arteriosclerosis, cerebral hemorrhage, brain tumor, or stationary general paralysis. Symptoms referable to the cranial nerves and spinal cord are usually lacking, and the fewness of the cells in the pia suggests the possibility of but few being found in the spinal fluid.

Lantern slides were shown illustrating the lesions described.

THE CO-EXISTENCE OF VISCERAL SYPHILIS AND ANEURISM WITH SYPHILITIC MENINGITIS.

G. Y. RUSK, M.D.

The material which I would present is intended to emphasize the syphilitic etiology of that form of chronic meningitis of which Dr. Dunlap has spoken.

The first case presented such a meningitis with gummata of the liver and an aneurism of the arch of the aorta. The second case shows aneurismal dilatation of the basilar artery and a saccular aneurism of the middle cerebral artery at its origin.

The role that syphilis plays in the etiology of aneurism we need not discuss, but its great importance is well recognized.

The first case was that of a woman forty-nine years of age;

of late years she had used alcohol to excess and in the last three years had used morphine for control of pain in her chest, due to the aneurism. She was admitted to Manhattan State Hospital in an acute hallucinatory state, which was due to use of drugs and which cleared up within a few days of admission. She died of lobar pneumonia. The principal anatomical findings I have already indicated and I refer you to the specimen of liver and aneurism.

The nervous system was negative in the gross, except for a slight but distinct haziness of the pia over the base. Microscopic examination showed a spotty infiltration of the pia at the base, with lymphoid and plasma cells; over the convexity the inflammatory elements were scarce, but throughout there was some increased cellularity of the pia, and a slight hyperplasia of the glia of the first layer of the cortex. A study of the principal vessel trunks showed a combination of endothelial proliferation in which there is some new elastic tissue formation with the changes of the ordinary atheromatous type. Sections from the medulla and cord similarly showed chronic meningitis of the same type and of moderate grade.

The second case of aneurism of the basal vessels occurred in a man of about fifty, who after a period of depression with defective memory, lapsed into a mildly demented state. There was slight muscular weakness with spasticity on the whole right side, due to pressure of the aneurism; there was no definite history of syphilis, but the patient had suffered from headaches for a long time before admission, and his pupils were unequal and reacted sluggishly to light. On the probability of former syphilis he was given a course of anti-syphilitic medication. He died about twenty-four hours after a hemiplegic attack.

At autopsy in addition to the aneurism there was marked thickening of the pia, especially over the base and extending over the frontal and parietal lobes. There were adhesions between the frontal lobes and granulations in the fourth ventricle.

Microscopic examination of the brain tissues in this case again showed a similar chronic meningitis of more severe grade and more diffusely distributed than in the previous case.

Study of the vessels showed in the main an advanced grade of atheroma, but one of the smaller vessels of the cortex in the frontal region showed, in addition to the atheromatous change, what appeared to be the remains of an old syphilitic endarteritis.

Lantern slides illustrating the gross brain condition in the second case and also gross preparations of the gummata in the liver and of the aortic aneurism were shown.

THE PATHOLOGY OF EXPERIMENTAL ANTERIOR POLIOMYELITIS IN THE MONKEY.

PAUL A. LEWIS, M.D.

(From the Laboratories of the Rockefeller Institute for Medical Research, New York.)

On behalf of Dr. Simon Flexner and himself, the author presented a series of lantern slides to bring out the following points developed in the course of their recent work with this subject:

I. The experimental disease in the monkey results in lesions of the central nervous system entirely comparable to those of the disease in human beings.

II. The characteristic feature of the early stages of the disease in the monkey is a perivascular infiltration with cells of the lymphocyte series. The infiltration is first seen in the pia-arachnoid and extends along this membrane and finally along the vessels into the gray matter of the spinal cord.

III. In neither the human disease nor in the monkey are the lesions strictly limited to the anterior horns. The lateral and posterior horns, the white matter, the spinal root ganglia and the pia-arachnoid are likewise involved.

A CASE OF PULMONARY, CEREBRAL, AND MENINGEAL BLASTOMYCOSIS.

G. Y. RUSK, M.D.

This case of blastomycosis occurred in a woman of sixty-three years who after a period of general feebleness, was a patient in one of the general hospitals in the city. She is said to have become confused and talkative, and was admitted to the Manhattan State Hospital. During her two weeks' residence she was in an almost continuous comatose state with occasional episodes of low-grade delirium. The autopsy showed a brain with diffuse pial haziness, slightly more marked over the base and over the cerebellum; gelatinous masses in the lung which will be described later; acute hemorrhagic cystitis. No skin lesion was present.

In the left lung situated near the root was a group of cavities varying from the limits of visibility to 3 cm. in diameter, filled with a sticky mucoid material; for the most part they appeared inclosed in a thin connective tissue capsule, the smaller cavities were less well defined; one passed externally from the area of the larger masses into an area of diffuse thickening of the tissue, in which were scattered tiny yellow foci, suggesting plugs in small bronchi with slight bronchopneumonia.

At the time of autopsy the condition was wholly unrecognized and the process suggested a new growth, most probably a colloid carcinoma, so no cultures were taken.

Sections from the lesions found in the lungs showed the main masses of gelatinous material to be composed of a budding organism with a large capsule lying in a mucoid matrix; the walls of these cavities showed a certain amount of fibrinous overgrowth, which the organism seemed to be gradually eroding, the lining cells becoming separated and swollen, and the protoplasm finely vaculated, while the nucleus became pycnotic and gradually disappeared. One must go some little distance into the tissue before one comes upon evidence of reaction and then one finds accumulations of lymphoid and plasma cells, probably fewer than one would expect, and a few multi-nucleated cells, but rarely is a definite giant cell seen in this region. When one passes to that part of the tissue described as diffusely firm, the microscopic picture changes considerably and one has all the elements of a chronic infective granulomatous process, including the formation of large giant cells, many of which contain parasites. Caseation is not found. Through the tissue large numbers of the organism are seen, singly and in groups. Occasional small hemorrhages are seen in the tissue. The bronchi both at the level of the first sections described and also in the second group contain parasites, and it is probable that this is the main method of dissemination in the lung tissue.

It is to be expected than an organism causing the tissue erosion, as described above, should make its way into the circulation; in the brain and meninges of this case we find the organism in great numbers.

Neither grossly nor on section, however, has any evidence of blastomycetes been found in the other organs.

In the brain the principal foci are found symmetrically situated in the basal ganglia and in the cerebellum, especially between the folia. Microscopically, however, additional foci are found in the basal ganglia, and in the cortex in a few places connecting usually with the pial invasion. The meninges particularly over the base running into the Sylvian fissures and also into the smaller fissures show a remarkable appearance. The organisms are frequently found in large masses or scattered singly; they are more or less mixed with the elements of the inflammatory exudate, lymphoid, plasma cells and large numbers of giant cells, many of which contain the organism. The meningitis is likewise marked over the cerebellum, the pons, medulla and cord again show the organism and the tissue reaction. In the lateral ventricles organisms are found with accompanying exudate.

As one passes from the base to the cortex there is a rapid diminution in the number of organisms and likewise of the reaction. Over the base where the exudate is most marked we find no tendency to tubercle formation or caseation. About the foci in the basal ganglia a moderate reaction occurs, but it is extremely local and consists of lymphoid and plasma cells.

Of interest also is the very marked hypertrophy of the glia of the superficial layers of the cortex which occurs in response doubtless to the meningitis. On the part of the vessels no reaction of the endothelium is noticed and the perivascular infiltration seems entirely part of the meningitis.

As to the organism itself, it appears as a simple budding form, no evidence being found of sporulation or of the formation of hyphæ. The organism in this case varies from those previously found in human infection in the large capsule, which is best seen in the Zenker preserved material, while in Kaiserling or plain formalin material it is often quite indistinct; both the gross lesions and the organisms strongly suggest the form which has been found in the horse by Frothingham, who describes a large single tumor the size of a man's head, which was diagnosed as a myosarcoma and which turned out to be a blastomycotic focus from which organisms were grown.

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DR. RICHARD M. PEARCE, *President.*

LESIONS OF THE CENTRAL NERVOUS SYSTEM.*

JOHN H. LARKIN, M.D.

Dr. John H. Larkin showed lantern slides illustrating some unusual lesions of the central nervous system.

1. The first specimen was taken from a three-year-old child and showed an absence of the cerebellum on one side. On the opposite side there was absence of the olive. The pons also showed marked indentation, and there was a corresponding recession in the whole bulk.

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*Presented to the Society, March 9, 1910; received for publication, April 19, 1910.

2. Specimen of the same case, higher power, showing condition of atrophy of the olive on the side opposite to that from which cerebellum was absent.

3. Section from side on which the olive was preserved.

4. Same section with higher power, showing normal contour of the pontine region on one side, but more or less loss on opposite side.

5. As is well known where there is congenital absence of the cerebellum, the atrophy goes beyond the pontine region, and there is atrophy of the brain. This specimen showed the deep part of the brain. The normal contour perfectly preserved.

6. A rather ordinary specimen of clot on the dura mater. Case of middle meningeal artery rupture not accompanied by fracture. Removed from a college student who was kicked in the head during a cane-rush. He had no serious symptoms, but was found dead in his bed the next morning.

7. Same case showing clot and dura removed, showing great compression of brain.

8. A case of rather unusual interest; an aneurysm of the basilar artery. Specimen was removed from an organist who was taken ill while on his way to church. He sat down on a stoop on Madison Avenue; he was taken to a hospital where he died. Autopsy showed an aneurysm of rather unusual size. The whole cerebellum had been rotated by pressure of the very large aneurysm. There were no pathological lesions in the brain. The cause of death was simply rupture of the aneurysm. The patient was thirty-four years old, and no history of syphilis could be obtained. This was perhaps one of the largest aneurysms Dr. Larkin had ever seen in the brain. It measured 1½ inches in the longitudinal direction and 1 inch in the transverse.

9. Brain showing tumor posterior to both optic nerves.

10. A rather interesting brain from a boy, fifteen years of age, suffering from a spleno-myelogenous leukemia. He was taken from the street to Roosevelt Hospital in a state of coma, and died shortly after. On autopsy the case was found to be one of typical spleno-myelogenous leukemia. There was a very

large globular thrombus in the brain, dilating the ventricle to a marked degree. The thrombus could be taken right out of the lateral ventricle.

11. Case of aneurysm at base of pons with laminated thrombus taking place from one or the other of the carotid arteries. Great dilatation of the ventricles of the brain. The patient was a man, thirty-five years of age, who was found on one of the docks. This was a remarkable condition on account of the size of the aneurysm and on account of the healing process and of the absence of symptoms.

12. Another section of same brain showing laminated clot. No evidence of syphilitic inflammation.

13. A condition which is common in New York: a case of pia arachnoid hemorrhage. This is frequently met with in cases of trauma and in alcoholic individuals.

Charcot has described a condition somewhat similar and undoubtedly due to miliary aneurysms. Syphilis plays a great part in this condition. Very often the condition is not connected with trauma and is without any evidence of fracture.

14. Syphilitic leptomeningitis. The contour of the brain is normal except at the cortical part where there is depression of the brain substance. The pia arachnoid and dura are densely infiltrated. The other viscera of this individual showed multiple gummatous infiltrations in the spleen, heart, and liver.

15. Arteries from same case. There is growth of connective tissue in the intima, which has broken down.

16. Acute anterior poliomyelitis, showing absence of horn cells.

17. Higher magnification; same absence of horn cells and proliferation of glia tissue.

18. Case of chronic poliomyelitis, which had gone on for two years. In an article by Ernst a similar condition is shown, which he classes as acute anterior poliomyelitis. In reality the condition is not acute, but is chronic. One could notice complete absence of the horn cells, as compared with the opposite side.

19. After the glia tissue commences to proliferate there is complete liquifaction.

20. Section shows higher power; absolute loss of horn tissue and proliferation of glia tissue. This is a condition which may differ very greatly in different parts of the spinal cord.

21. A rare specimen of which only four cases have been described. Case of myelomalacia of the cord, somewhat approximating Landry's paralysis. The specimen was interesting because scattered all through it could be seen irregular hemorrhages. There were thrombi in the large veins, and the outline of the anterior horns in cord was entirely lost. There was thrombosis of some of the smaller veins. At different levels of the cord the condition differed very markedly. The anterior horn and bulbous condition of the posterior column could be noof hemorrhage. At the spinal pia there was acute exudative inflammation, in some places polynuclear in type. The whole condition was one of myelomalacia due to venous thrombosis.

22. Specimen of caisson disease. Disintegration of the horn and bulbous condition of posterior column could be noticed. This also was a condition which might differ markedly at different points and levels.

23. Ordinary case of hemorrhage of brain caused by a blow on the opposite side.

24. Section from same case.

25. Case of confluent hemorrhage from blow on top of head.

26. Case of hemorrhage of brain, of three weeks' standing.

27. A somewhat common condition, known as pontine hemorrhage. Pontine hemorrhage seemed hard to explain, and on studying the anatomy it was difficult to see why such large hemorrhages should occur in the pontine region. In some cases there were very few symptoms, in other cases the symptoms were cerebellar in character. This individual had entered the hospital with symptoms which pointed to a cerebral tumor. At operation 20 c. c. of dark fluid were drawn from the cerebrum. The pa-

tient died shortly after. At autopsy no cerebral tumor could be found, but there was a great mass distending the pontine region. Dr. Larkin suggested that possibly a number of cases of pontine hemorrhage were not hemorrhages in the ordinary sense of the word as applied to other parts of the body, but depended upon a congenital condition.

28. Section of cavernous angioma of the pons of exactly the same type as that found in the liver.

PERIOSTITIS ALBUMINOSA.

JOHN A. HARTWELL, M.D.

This condition was first described in a paper by Poncet,[1] published in 1874, from a study of cases seen by Ollier. Poncet described the clinical and pathological picture of the disease, gave the name of periostitis albuminosa to it, and considered it as a specific disease having no relation to other periosteal or osteal disease. Schlange,[2] in 1887, expressed the view that the disease is similar in etiology to suppurating periostitis, and that the peculiar exudate represents a degenerative change from the pus exudate, possibly because the infecting organism is attenuated. Volkmann, Kocher, and Tavel agree essentially with this view. Vollert,[3] in an extensive study of the exudate, comes to the same conclusion. Bourlot[4] made an analysis of forty-eight cases. Of these he classed two as traumatic, three as tuberculous and forty-three as staphylococcic in origin. His view was that the disease was essentially the same as osteomyelitis, only differing from it in the nature of the exudate, and that this difference was due to the fact that the infecting organism was of a low grade of virulence. He compared the two from etiological, clinical and bacterial standpoints and demonstrated their close relation. Caillebar,[5] on the other hand, insists that all the cases are tuberculous in origin, and that the exudate is similar to the exudate occuring in tuberculous irritation of serous membranes throughout the body, and often seen in cold abscesses from bone and the soft parts. These selections from the literature, which is not extensive, express the various views as to the nature of the process.

The pathological anatomy of periostitis albuminosa does not differ essentially from other forms of periostitis, except in the peculiar exudate which gives to it its name. The irritating organism may be present in the bone itself, or it may be confined to the periosteum. Some writers have believed that the outer layers of the periosteum only were affected, but the greater number believe the condition to be subperiosteal in origin. Sections of the periosteum show the same inflammatory changes as are present in suppurating periostitis. The exudate, however, differs from pus. It is often free from any cellular elements. It varies in consistency from a thin syrupy fluid to a gelatinous mass. It is transparent and straw-colored, or slightly more yellow. It contains a high percentage of proteid, often 3 per cent. and often coagulates spontaneously, this apparently depending, however, on the presence of leucocytes containing the prothrombin. The fluid is often large in quantity, and frequently forms a cyst-like cavity for itself in the soft parts. The soft tissues surrounding the bone usually show a marked inflammatory reaction to the irritation. The condition is rare, and we can find only two cases reported in the English literature, one on the dorsum of the fourth finger reported by Edington,[6] and one by Dupuis[7] occuring on the tibia following an injury. Neither gives bacteriological findings. The following three cases coming under our notice during the past two years are deemed worthy of report:

F. S., on admission to the hospital gave a history of a swelling appearing in the lower third of the left thigh about one month previously. No cause for this was known. The swelling was slightly tender and painful when walking, and there was some disability of the left knee.

Physical Examination.—Gave some indefinite evidence of pulmonary tuberculosis. The lower two-thirds of the left thigh were uniformly enlarged down to the knee joint, being three inches larger in circumference than the right thigh at corresponding points. The swelling interfered with the muscles in such a way as to prevent full flexion of the knee. It was slightly tender to pressure, and just above the internal condyle of the femur the skin was slightly reddened and here was the maximum tenderness. To palpation, the swelling was hard, and gave the sensation of a fusiform growth attached to the femur. It was slightly more marked on the internal aspect than on the rest of the circumference.

Operation.—Incision was made over the inner aspect of the thigh, about three inches above the internal condyle. This was carried down through the muscles and a large quantity of thick, gelatinous fluid evacuated. It seemed to come from the medullary canal of the femur, through two fistulous tracts. A portion of the sac was removed for examination. It proved to be muscle tissue showing marked histological changes, of an inflammatory nature. The fluid planted on culture media gave a growth of staphylococci. The wound failed to heal and two weeks later the thigh was opened on its external aspect and in carrying the incision down to the femur a large bone-like mass grew like a plate from the posterior surface of the bone, and spread out into the muscle tissue. It was separated from the soft parts by blunt dissection, and from the shaft by chisel leaving an apparently normal shaft intact, with the periosteum separated from the posterior aspect. It was then seen that what had been taken for fistulous tracts into the femur were, in reality, holes through this plate of bone. Subsequently the man made a good recovery.

Pathological Report: (By Dr. Charles Norris).—The specimens removed at the first operation were small and unsatisfactory for diagnosis. At the second operation a considerable amount of tissue was removed consisting of muscle tissue and small and large bone plates and spicules. A half a test-tube full of clear yellowish fluid was sent to the laboratory; this fluid clotted spontaneously in the course of half an hour. The examination of the various pieces show in the main an acute inflammatory process, varying, however, in different places as to histological detail. The muscle has undergone extensive hyaline degeneration. Some of the muscle cells show evidences of regeneration as indicated by multiplication of the nuclei. Many pieces, on section, seem to be made up of an edematous and very highly vascular tissue, the seat of extensive hemorrhagic and inflammatory edema. The serous exudate is in many places rich in plasma cells, with a small number of polymorphonuclear cells. In other places, the inflammatory process is less acute in character, showing small and well circumscribed areas of small round cells and more or less dense masses of irregularly fragmented nuclei.

The pieces containing bone present a beautiful example of an active formative osteitis; the marrow spaces are lined with rows of osteoblasts and are filled with proliferating marrow tissue, showing numerous fibroblasts. This tissue without definite bone formation is extensive and in places so cellular in character that it gave rise to a question as to whether or not we were dealing with a pure type of ossifying periostitis. The clinical and *x*-ray features of the case seemed to lend support to the possibility of a tumor. The final diagnosis of the condition is ossifying periostitis of the femur with inflammatory lesions in the adjacent muscle and tissue. The term periostitis albuminosa refers to the character of the fluid obtained at the operation. The formation of fluid of this character is an expression of irritation of the periosteum.

We have placed under the microscope a section obtained from a case of sarcoma of the lower end of the tibia, which was treated with radium tubes by Dr. Abbe. The collection of fluid was under the periosteum of the lower end of the tibia in this case and was similar in character to that described in the case above. The formation of this fluid in this case was possibly due to the presence of a suppurative cellulitis resulting from the insertion of the radium tubes, the fluid having collected under a part of the periosteum not yet apparently involved by the growth. An important point to remember in diagnosis, is that the mere presence of such fluid does not exclude the possibility of a new growth.

W. P., male, age forty-eight. Gave a history of having noted a swelling in the upper end of the left tibia, which appeared about two years before, but it had given him no particular annoyance till he fell and struck it about three months before his admission to the hospital. Examination showed a fluctuating mass about the size of a small orange occupying the upper anterior part of the interosseus space of the leg. It showed the external evidences of being inflamed.

Operation.—An incision into the mass evacuated a thick, gelatinous, semi-transparent fluid. It seemed to be encapsulated in a cystic wall. The patient remained well for nearly a year, when the swelling recurred, and this time it grew rather rapidly to its original size. It was again incised, and a cavity containing about eight ounces of a transparent gelatinous material, varying in consistency from egg albumin to jelly, and of straw color, was found. This substance seemed to lie in a cavity bounded by the tibia, interosseous membrane, the fibula and the tibialis anticus muscle. There was no true sac. On the outer aspect of the tibia, near its head, was a roughened area denuded of periosteum, and the periosteum surrounding this was much thickened. A distinct bridge of bone grew from the tibia outward to the fibula resembling the bone plate described in the first case. The roughened surface of the tibia was curetted; the lining of the cavity was cauterized with carbolic acid, and firmly packed with gauze. A complete healing apparently took place.

The pathological examination of some of the wall of the cavity which was removed showed only chronic inflammatory changes. The bacteriological examination is not recorded. The Wassermann reaction for syphilis was positive in this patient.

D. M., age thirty-two. Suffered from typhoid fever in the fall of 1908. During his convalescence a painful swelling appeared over the outer side of the lower end of the humerus which was diagnosed as a periostitis. It never entirely subsided, but gave him comparatively little trouble for six months. Then it grew more rapidly and became painful. At the same time a second focus appeared over the subcutaneous surface of the tibia.

Operation.—These were both opened in June, 1909. The lesion on the arm was found to be an osteomyelitis and periostitis involving the lower end of the bone. About six ounces of the same kind of fluid as was found in the other cases was present, though it was slightly more turbid. The periosteum was thickened and separated from the bone for some distance. On opening the medullary cavity the medulla was found to be slightly purulent. The swelling over the tibia was incised, and gave exit to a similar fluid, but there seemed no involvement of the bone itself.

Pathological examination of the bone and the medullary substance from the humerus showed the changes of a subacute osteomyelitis. The fluid contained pus detritus. No bacteria could be demonstrated in it, and no growth developed on culture media.

These three cases are typical of the disease. They all involved the long bones. They all showed the characteristic fluid. They were all chronic. They all involved the under surface of the periosteum. Two involved the periosteum only, while one involved the medulla also. One showed a staphylococcus, one was sterile and the third is not recorded. One occurred without previous disease, one was in a syphilitic subject, and one developed following typhoid fever. They would seem to demonstrate, so far as they go, that periostitis albuminosa is not a specific disease, but is an expression of an irritation of the periosteum by an infecting organism of a low grade of virulence which produces the characteristic albuminous exudate rather than true pus. We have no knowledge of why this is so.

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THE LESIONS OF CHRONIC ARTHRITIS.

E. H. NICHOLS, M.D.

Pathologically there are two types of changes in chronic arthritis; the first type begins as a proliferation of the connective tissue of the joint, chiefly in the synovial membrane and perichondrium, and tends to destroy the cartilage and lead to ankylosis of the joint; the second type begins primarily as a degeneration of the joint cartilage, and leads to deformity, but not to ankylosis.

There has been a great deal of confusion as to the nomenclature of the cases of chronic arthritis due, first, to the difficulty in determining the primary cause of the joint lesion. In each of the types there occurs a series of changes, and in each step of each series there may be a different clinical picture. Moreover, there has been a failure in most cases to study the pathological lesions in connection with the clinical case. Confusion also has been caused by a study of the cases solely from the point of view of the *x*-ray.

Although there are two types of lesions in these cases of chronic arthritis, it must be remembered that these two types do not correspond to two definite etiological factors. Many different causes may produce changes of the proliferative type, and many different causes may produce changes of the degenerative type. The only one cause producing both types, so far as my experience goes, is trauma. Moreover, one cause can produce a great variety of gross appearances and of clinical symptoms, and many causes can produce the same type of pathological changes. Another thing, the primary cause may produce partial injury to the joint, this primary injury may produce continued injury, and so the process once started may continue in a vicious circle forever.

Attention must be called to the fact that there are comparatively few structures in the knee joint. They are bone, cartilage, synovial membrane, the bone covering or perichondrium, the membrane covering, the trabeculæ, i. e., the endosteum, and the bone marrow.

The proliferative type of joint lesion begins chiefly as a proliferation of the synovial membrane. Many causes may produce this proliferation. It may follow pyogenic infection. Infection with the gonococcus may produce lesions of this same type; the same process is seen in the so-called Still's disease; it may appear in single or in many joints in which there has been no bacterial infection; it has occurred in syphilis, and, finally, it may follow fracture. It occurs in young people and in older patients; in one joint or in many. There are undoubtedly many cases, the cause of which cannot be determined by our present methods.

There are many theories in regard to the origin of this type of arthritis. Some say that these cases are practically always of bacterial origin; some consider the cause to be faulty metabolism. In many cases it is impossible to demonstrate bacteria, though the gonococcus does cause some of these lesions. The pathological lesions point toward the probability of the theory of "faulty metabolism."

The process is as follows: a proliferation of the synovial membrane occurs, forming a layer of synovial "pannus" which grows across the surface of the joint cartilage. It may grow over both cartilages, and then these two layers may unite and lead to adhesions, or as the synovial membrane extends over the joint cartilage it may project down into the cartilage and lead to destruction, so that ultimately the bone is denuded of cartilage. Ultimately in some cases the entire joint cartilage is destroyed by this pannus.

Proliferation of connective tissue also occurs in the marrow spaces of the epiphyses, and connective tissue forms. Ultimately this proliferated connective tissue may perforate the cartilage from below, and the pannus from the epiphysis may come into contact with the pannus from the synovial membrane, so that ultimately the entire amount of cartilage may be destroyed.

Besides these two destructive processes, proliferation of the synovial membrane and of the connective tissue, there may be proliferation of the perichondrium and of the endosteum. These two processes represent an attempt at repair and lead to new formation of cartilage and of bone. In the perichondrium the proliferation may begin in the middle of the joint so that when the joint is opened there are besides the extension of the pannus over the surface of the cartilage, raised, projected, rounded areas, due to thickening of the perichondrium, or the thickened perichondrium may at first form a rather thin, reddish looking membrane on the surface of the joint, and may later form islands of bone which may become fused with the epiphysis.

Just as there comes proliferation of the connective tissue of the marrow with the pannus, so with proliferation of the perichondrium there may be proliferation of the endosteum. This may lead at first to mere thickening of the trabeculæ, or it may accompany the new growth of connective tissue in the marrow space of the epiphysis. The changes may go on so as completely to destroy all of the original cartilage, all four layers ultimately uniting and forming complete bony ankylosis with complete destruction of the original line of joint articulation.

Hence, there are four different layers of tissue involved in this process of destruction and repair. Two of the processes represent reaction to injury, two are true reparative processes which, however, lead to destruction of the joint.

Very early in the disease there comes, as shown by *x*-rays, an apparent atrophy of the bone in the vicinity of the articulation. Microscopical examination of a great many of these cases shows that there is practically no resorption of the bone of the epiphysis by giant cells; on the contrary, there is in many cases a new formation of bone. The apparent atrophy is due probably only to a removal of the lime salts. The so-called atrophy of the early stages is not a true bone resorption.

As regards the capsule, there is here usually a proliferation of the connective tissue, which may vary from young granulation tissue to an excessive amount of dense fibrous tissue. The form varies according to the etiological factor. There may also be formation of the so-called synovial tags. This is, however, very rare and much less marked than in the second type of degeneration. In the degenerative type mobility of the joint is maintained, and the joint is not destroyed. In the proliferative type ankylosis occurs early usually, and there is no chance for the development of these "joint mice."

In the other type, the so-called degenerative arthritis, the process is entirely different. It begins primarily as a degeneration and softening of the articular cartilage, with no sign of inflammation in the early stages. There may be a little inflammation later, never any of consequence. As in the proliferative type, many different causes produce these so-called degenerative cases. These changes are certainly more common in old people, in women, and in workers, than in others. This type of change may appear secondary to deposits of gout urates in the joint. It may occur in organic disease of the central nervous system, may follow trauma, or may follow fracture of the joint with great displacement of bone. The proliferative type may also follow fracture, but it is always fracture with but slight displacement. It may occur also in osteitis deformans, and in the vicinity of tumors, even without perforation of the tumor into the joint cavity.

The first change seen is a fibrillation of the articular cartilage. The constant motion of this fibrillated and softened intercellular tissue of the cartilage leads to steady erosion of the articular facets. The process may go on until the joint cartilage has been entirely softened, eroded and removed. The endosteum of the epiphysis may be thickened about the trabeculæ and so the marrow spaces may be filled up, and ultimately the ends of the bone may become thickened. As a result of these three changes, softening, destruction of cartilage, and erosion, there may occur a change in the contour of the joint, which in some cases may become extreme, but never leads to ankylosis.

Besides this fibrillation and erosion with destruction of the articular facets, there comes another change. The change takes place inside the capsule, which becomes thickened with the formation of fibrous tissue and consists in the formation of islands of cartilage by proliferation of the perichondrium at the margin of the joint; ultimately these islands of cartilage may be converted into true bone. This true bone may be entirely denuded of cartilage.

So far as the capsule is concerned there is usually only moderate thickening, although it varies from the usual type. In Charcot's disease there is usually tremendous thickening of the capsule itself.

In these joints there is one interesting change, that is, a frequent formation of synovial tags. These tags may be formed of granulation tissue or of dense masses of cartilage or of masses of bone. Such masses may be torn off and set free in the joint cavity, as joint mice, etc. In a certain number of cases these masses are sessile and in some cases they are in the thickness of the capsule itself and not in the cavity of the joint.

So that from the cases which have been examined, it may be said that anatomically there are two types of lesions, the first beginning as a proliferation of the synovial membrane, leading to destruction and ankylosis of the joint; the other beginning primarily without inflammation as a degeneration of the joint cartilage leading to deformity of the joint without ankylosis. In either type the process tends to continue in a vicious circle.

Clinically the physician's object should be to recognize the type of lesion present; then, in specific cases, to recognize, if possible, the original etiological factor, and, when possible, to remove it.

The nomenclature used is one which seems satisfactory because it describes the pathological type of lesion. For the present the use of these two terms seemed to afford a chance for the diminution of confusion, because in all cases one would know which type of joint was being described.

Discussion.

Dr. W. R. Townsend expressed his inability to add anything to the pathological study of the subject, but he thought that if the last word could be said as to the nomenclature of the disease from a study of its pathology, a great deal had been accomplished. The simple division into degenerative and proliferative arthritis was certainly very welcome. From the clinical standpoint the question was one with which he had had some experience. It had always seemed to him that some of the changes in the joints were related to the question of weight bearing and use, and this was well illustrated in two *x*-ray photographs which he presented. The patient was a man of forty-two years of age who undoubtedly had a Charcot joint. This man was very active, and in the short space of four weeks, between the time of taking the first and the second photographs, there occurred complete erosion and separation of the head and neck of the femur. Had the joint been kept quiet and motion prevented, one would not expect the disease to prove so rapidly destructive. The arrest of such a process, he thought, was often due to the complete rest which these patients had in the hospital; and this was further evidenced by the way in which many of them rapidly grew worse after discharge. The question of prognosis was always interesting, and if, after further study, it could be determined with a reasonable amount of certainty what could be predicted for the future in the different types, another great step forward would be made. To be able to say, from a study of the clinical symptoms aided by *x*-ray pictures, that a given case would or would not improve and bony or fibrous ankylosis would or would not occur was of value.

Dr. Rufus Cole said that he very much appreciated Dr. Nichols' description of the lesions seen in cases of arthritis deformans. He understood that Dr. Nichols felt that no close relationship could be determined between the different types of lesions and the various etiological factors concerned, though he understood that Dr. Nichols felt that the degenerative type is less frequently the result of an infection than is the other type Certain experimental work which Dr. Cole had done, he thought, had a bearing on this question, as bringing quite positive proof that the degenerative type *may* be produced by infectious agents

Several years ago, when studying the question of arthritis in rabbits, as produced by injections of streptococci, the lameness persisted in one rabbit for several months. On examining the joints of this rabbit and making an x-ray examination, a definite bony thickening with exostoses was found. The rabbit was killed and the examination of the joint showed eburnation, exostoses, and lipping of the bones, as seen in the degenerative type as described by Dr. Nichols. This case, therefore, apparently offered good proof that, under certain conditions at least, bacteria may give rise to lesions of the degenerative type.

FURTHER STUDIES OF SARCOMA OF BONE.[1]

LEO BUERGER, M.D.

What with the knowledge of the structural changes in bone that can be gained by means of the Rœntgen ray, and what with the aid of the newer viewpoints in the histopathology of sarcoma, we are in a position to-day to acquire a much more thorough and comprehensive conception of the method of growth of sarcomata of bone than has been possible in the past. In a previous publication,[2] giving observations on twenty bone sarcomata, certain characteristic features were described and their importance in diagnosis was pointed out; the utility of adhering to the histologic classification of Borst was demonstrated and a tentative grouping into seven types, each distinguished by certain definite gross morphologic criteria, was suggested as being at least of some temporary value. Since that time my own experience has been enriched by a number of additional clinical cases; two more specimens of sarcoma of the long bones have been

[1] From the Pathological Laboratory of the Mt. Sinai Hospital, New York. Published in full in the *American Journal of Medical Sciences*, September, 1910. Figures were shown at the meeting. (Demonstration by lantern slides.)

[2] *Surg., Gynec., and Obst.*, October, 1909, pp. 431-461.

studied, as well as two cases of multiple myeloma. The very excellent account of Rumpel's[3] radiographic findings in bone sarcoma has been compared with the data acquired by x-ray and anatomic investigation of my own material, so that I am able to give a review based on some thirty clinical cases and forty-six specimens.

Ribbert, in his admirable inquiry into the development of these tumors, has shown that many of our old notions, particularly in regard to genesis, ought to be abandoned. Our own experiences are, in the main, in accord with his, especially in so far as they concern the probable seat of origin; but they are at variance with his conclusion in the matter of the site of inception of the so-called "peripheral" growths. We shall revert to this later on.

From a consideration of the many data before us we are led to an endorsement of a view recently advanced; namely, that true "periosteal" sarcomas are probably so rare as to be negligible, and that the bone sarcomas find their incipiency in a focus somewhere within the confines of the osseous tissue or perhaps just under the periosteal covering. Leaving aside the arguments in favor of this opinion for the present, let us assume the beginnings somewhere within the peripheral layers of the substantia corticalis, in the medulla, in the corticalis itself, or in the spongy bone, and the following structural changes will be seen to take place. There will be a disintegration and disappearance of the osseous tissue and marrow *pari passu* with the enlargement of the sarcoma, although in the case of certain varieties new bone formation either on the part of the tumor or on the part of the irritated normal bone elements may occur. The method of advance will vary in the way to be described later. Here it suffices to note that sooner or later the heterotypical cells will have destroyed some of the cortex and have found their way under the periosteum which they will lift off as they multiply. By virtue

[3] RUMPEL: Uber Geschwülste und entzündliche Erkrankungen der Knochen im Röntgenbild. Hamburg, 1908.

of this detachment (and possibly also because of the stimulation of the tumor cells themselves), proliferative changes are induced in the bone covering, and new osseous lamellæ are laid down. In the earliest stages this forms a bony thickening over the cortex indistinguishable from an inflammatory periostitic deposit. Soon, however, the neoplasm tends to encircle the bone carrying the periosteum with it. A fusiform tumefaction results, the ends of the spindle presenting on section characteristic wedges or triangular areas of periosteal bone. Later the periosteum, too, is broken, and its remnants with attached portions of new-formed bone may become included in the tumor.

In this short characterization it has been deemed advisable to call attention only to a very few but essential facts, namely: the origin in the bone tissue or marrow; the destruction of the bone and the role of the periosteum; for these will aid in the detailed study now to follow.

Turning our attention to the comparative study of our own twenty-two specimens and of the twenty-four described by Rumpel, we shall find that the tentative grouping proposed by me is also of service in classifying the tumors portrayed in that author's Atlas of Radiograms.[4] The following is the grouping under discussion.

A. *Central (Endosteal) Tumors.*

1. Expansive of the bone ends.
2. Expansive of the shaft.
3. Diffusely infiltrating (non-expansive).
4. Destructive, dissolutive (non-expansive).
5. Sclerosing (calcifying).
6. Perforative (non-sclerosing).

B. *Peripheral.*

7. Subperiosteal and true peripheral.

1. *Expansive Tumors of the Ends of Long Bones.*

Exquisite examples of this form are the giant-celled sarcomas usually encountered in the lower end of the femur and upper end of the tibia and humerus. They begin, as a rule, in the spongiosa of the diaphysis, not far from the epiphyseal line and exhibit a marked tendency to bring about complete disintegration of the osseous tissue. By virtue of necrosis, liability to hemorrhage, and regressive metamorphosis, larger or smaller cavities are produced. As for their "expansive" nature, this needs qualification, since it is often more apparent than real. Although a moderate amount of enlargement of the extremity of the bone may be produced by the tumor or growth, even before the investing cortical sheath has been invaded, this is but meager when compared with the dilatation incident to the later destructive changes. Complete erosion of the corticalis is the result when the tumor attains considerable size. The periosteum, however, may remain as an encapsulating vestment, and hand in hand with its recession from the surface, there occurs the development of new bone, so that a new shell of thin osseous lamellæ may form the chief covering of the neoplasm. The egg-shell or ping-pong ball[5] crackle, therefore, may be elicited by pressure on either rarified cortex or new formed periosteal bone.

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[4] loc. cit.

It is these tumors that may be easily confused with bone cysts. If we remember that cysts do not perforate, but cause rarefication and expansion of the cortex, that they are surrounded by a smooth bony wall and that reactive bone proliferation either in the bone itself or on the part of the periosteum does not occur with them, we shall have at our disposal a sufficient number of data for differential diagnosis.

That other forms of cystic sarcoma (myxo-sarcoma) and more malignant varieties (osteoblasto-sarcoma) may also belong to this group, I have already mentioned elsewhere.

2. *Expansive Tumors of the Shaft.*

A brief mention of the occurrence of expansive tumors in the diaphysis will be enough to acquaint us with this type. In

[5] Suggested by Dr. Bloodgood.

my series there was a chondro-sarcoma of a metacarpal bone and one of the femur. In Rumpel's list there was a sarcoma developing in an enchondroma of the humerus which had much in common with my specimen of the femur. The same picture of bone destruction that is seen in the last type occurs here. The available material is hardly adequate to allow of formulating any definite rules as to what radiographic pictures ought to be expected. It is evident, however, from the data at hand, that some difficulty in the differentiation between benign enchondromas and chondro-sarcoma can hardly be avoided. In the enchondromas we not rarely encounter multiple tumors that cause disappearance of the osseous tissue leaving a structure which in the *x*-ray picture has a speckled and rarefied appearance. The absence of periosteal deposits is one of the most important aids in distinguishing them from many of the types of central sarcoma of bone.

Two other conditions that may simulate the central expansive sarcomas of the shaft may be mentioned: bone cysts, and cyst formation in so-called "osteitis fibrosa." The enchondromas and bone cysts both from the clinical standpoint and from the skiagrams, may be practically identical, so much so that a close genetic relationship seems not unlikely. Indeed, the bone cysts are, in all probability, the end result of a number of different types of endosteal bone disease. It is not my purpose here to enter into a discussion of the differential diagnosis between these conditions and sarcoma, inasmuch as this can be best treated from a consideration of a large number of radiographic plates. Here it may suffice to call attention to the following points: that in bone cysts, fusiform or pyriform bone expansion, rarefication of the substantia compacta with the greatest absorption at the equator of the tumefaction and a distinct, a regular line of demarcation between cyst and bone tissue, are characteristic; whereas irregular expansion, perforation, extraosteal masses, periosteal bone deposits, and irregular contour are more apt to be amongst the qualities of the malignant growths.

3. *Diffuse Infiltrating* (non-expansive) *Tumors.*

Quite a contrast to the last described series is presented by those sarcomas that probably originate in the innermost layers of the substantia compacta or in the medullary substance, when they develop in the shaft, and probably begin in the *spongiosa* when they belong to the extremity of a bone. Here expansion of the corticalis is missed, and we find a displacement of osseous tissue and marrow, with marked tendency to intramedullary extension. We are often surprised, on section of the bone, to see how far in the longitudinal direction the tumor growth has advanced.

This type ought to be recognized as of clinical importance inasmuch as an early diagnosis will hardly be made. For the endosteal tumor may have already replaced a large portion of the medulla and innermost layers of corticalis, or may have caused pathological fracture long before a suspicion of neoplasm is entertained. Thus the diagnosis was made after spontaneous fracture in one case, after osteotomy in two cases, and after careful radiographic examination and exploratory incision in a fourth case. The patients do not usually consult us until after considerable bone destruction has taken place.

4. *Destructive, Dissolutive Tumors.*

When a sarcoma becomes so highly destructive that there is rapid dissolution of the whole region surrounding its point of origin, and when there is neither a tendency to expansion nor to demarcation of the neoplasm, we have a growth which may be grouped under "destructive," or "dissolutive tumors." I have seen some half dozen such sarcomas of the upper end of the fibula. The invasion of the surrounding soft parts occurs early and the tumors usually pursue a very malignant course. Rumpel's series affords two such specimens, one of the upper end of the tibia, another of the upper end of the fibula.

5. *Sclerosing, Calcifying* (ossifying) *Tumors.*

Perhaps one of the most interesting varieties of bone sarcoma is that in which an osteoid or chondroid matrix is elaborated. Hand in hand with this higher differentiation into a typical bone and cartilage producing mesoblastic tissue goes a tendency to sclerosis, in the sense that larger or smaller areas of the tumor are converted into stony masses. This is accomplished either by a sort of lawless calcification or by the deposition of lime in the osteoid matrix and the consequent production of a typical bone. Having already had six examples when writing my last paper[6] (three of the femur, two of the tibia and one of a rib), the histological and gross characteristics were sufficiently dealt with at that time.

When these tumors make their way out under the periosteum they give rise to the same bone proliferation seen in the other varieties, except that we must expect an additional osteogenetic process in the basal portions of tumor, namely, that which rides on the shaft of the bone. In the extraosteal tumor spindle the typical radiate arrangement of bony spicules is sometimes developed, especially in the chondroid varieties. That this feature is not a distinguishing characteristic of the "periosteal" tumors—as was formerly supposed—but belongs rather to those central tumors that simulate the periosteal variety becomes evident to us from our analysis.

In my own collection the calcifying and ossifying type was represented only by the osteoid and chondroid varieties, although in one of the round and spindle celled tumors a fair amount of irritative bone proliferation—on the part of the normal bone—was rather striking. Rumpel pictures marked sclerosis in a spindle celled sarcoma. Bearing in mind the fact that the sarcomas with specialized intercellular substance, such as the chondroid and osteoid, may, in the course of their growth, revert to immature, low types (spindle and round celled forms), and that we not infrequently find soft immature sarcoma in the metastases and extraosteal masses, it seems possible that osteoid or chondroid substance may be overlooked if the central portions

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[6] loc. cit.

—or the oldest parts—are not subjected to histological examination.

VI. *Perforative Endosteal Tumors.*

Instead of a large central focus causing expansion, or diffuse endosteal infiltration, or extensive bone destruction, or sclerosis, we may see a totally different picture: namely, a small intraosteal mass causing early perforation. In the analysis of Rumpel's sarcomas it was found that this type is not at all unusual. Seven of his tumors could be placed into this class, two of the tibia, two of the humerus, and three of the femur. In all of them the sarcoma had its origin in the spongiosa of the diaphysis and there was a relatively small endosteal focus with large extraosteal masses. The other features already sufficiently described can be readily detected by a glance at the illustrations.

We need hardly emphasize the difficulty and, in most cases, the impossibility of diagnosticating this type of sarcoma before perforation has taken place. When the humerus is affected, the recognition of the condition, even with radiograms, may tax our powers to a still greater degree. The meager changes in the bone may go with considerable tumefaction of the soft parts and the diagnosis of arthritis may be made.

VII. *Peripheral Tumors.*

Having had but one tumor whose origin was either "subperiosteal" or in the outermost lamellæ of the cortex, it would have been audacious to have expressed myself decisively in regard to the moot point of periosteal or peripheral origin in my first paper.[7] Comparing my own specimen with those described by Rumpel, the conclusion is inevitable that a certain percentage of the bone sarcomas do belong to this class, and that in a series of eight tumors, at least, the periosteum, although affected by the growth, is not the seat of its inception.

Is it always possible to distinguish the lesions of sarcomas of small extent from those that belong to a traumatic or inflam-

[7] loc. cit.

matory periostitis, in skiagrams? The differential diagnosis may be difficult, for the shadow pictures may show only periosteal deposits without appreciable changes in the bone itself. The circumferential type of bone deposit usually speaks in favor of neoplasm, whereas in the traumatic periostitis we are more apt to find irregular, and possibly multiple, patches of bone deposit. However, it is clear that, even in sarcoma, the very earliest periosteal lesion will not have encircled the shaft, and the beginnings of the neoplastic lesion may, therefore, be difficult of diagnosis.

General Considerations.

Having thus outlined the characteristics of forty-six bone sarcomas, and having grouped them according to gross morphological traits, it may be well to gain a broader impression of the subject by tabulating both our own specimens and those of Rumpel and by giving the subject of classification and point of origin more critical consideration. The distribution was as follows:

	Rumpel.[8]	Author.[9]	Total.
Femur	8	11	19
Tibia	5	4	9
Humerus	6	1	7
Fibula	2	4	6
Metacarpal	1	1	2
Radius	1	0	1
Ulna	1	0	1
Rib	0	1	1
Total	24	22	46

In order of frequency we would have femur, tibia, humerus, fibula, and metacarpal. Reinhardt[10] collected fifty-four cases in which there were nineteen of the tibia, eighteen of the femur, thirteen of the humerus, and two each of the fibula and radius.

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[8] Includes only those critically studied by me, the data being sufficient.

[9] The multiple myelomata are not added. Only specimens which were studied anatomically were included in my list.

[10] *Deutsche Zeitsch f. Chir.*, 1897, Vol. 47, p. 523.

Muller,[11] in reviewing two hundred and nine sarcomas, found the tibia affected seventy-seven times, femur seventy, humerus thirty-eight, radius eleven, ulna six, and fibula eight. The tibia and femur, therefore, take the first place, followed by the humerus, and then by the fibula and radius.

Has the comparative study of this larger number of bone sarcomas given impressions that would tend to strengthen notions already obtained through our previous investigation? We must answer in the affirmative. A suspicion has arisen that perhaps certain of the groups do not possess any essential properties with which the gross alterations are inseparably linked, and that the changes of bone architecture depend for the most part on variations in the site of origin of the neoplasm. However this may be, the establishment of the existence of important widely variant forms is not nullified; and we must concede, that, although the assumption as to the effect of origin may be true in the case of the "border-line" tumors, most of the neoplasms possess a sufficient number of distinctive qualities to allow of the grouping adopted by us. Tabulating Rumpel's tumors and my own, we find the forty-six sarcomas grouped as follows:

I. *Expansive of the Extremities of Bones.*

	Rumpel.	Author.
Femur	2	3
Humerus	1	..

II. *Expansive of the Shaft.*

Humerus	2	..
Femur	..	1
Metacarpal	..	1

III. *Diffuse Infiltrating.*

Femur	..	2
Tibia	..	1
Humerus	..	1
Ulna	1	..

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[11] Muller, Wilhelm.

IV. *Dissolutive* (destructive).

Fibula	1	3
Femur	..	1
Tibia	1	1

V. *Sclerosing, Ossifying, Calcifying.*

Femur	1	3
Tibia	1	2
Rib	..	1

VI. *Perforative Endosteal.*

Femur	3	1
Humerus	2	..
Tibia	2	..

VII. *Peripheral.*

A. Subperiosteal[12] (shaft)	1	1
B. True peripheral:		
Femur (shaft)	1	..
Humerus (shaft)	1	..
Radius (shaft)	1	..
Tibia (shaft)	1	..
Fibula (shaft)	1	..
Metacarpal (shaft)	1	..
Total	24	22

Rather striking is the large number of perforative endosteal tumors of which I have had but one example, and of which Rumpel—if my interpretation of his radiographic findings is correct—has had seven. This augmentation in the number of examples of a type which had to be separated from the rest in my series (although there was only one) makes it certain that this variety is to be reckoned with. None the less remarkable—and a circumstance which has somewhat altered my former concept—is the large proportion of peripheral sarcomata, seven out of twenty-four, as compared with one out of twenty-two in my list.

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[12] With very slight or practically no erosion of the substantia corticalis.

In the bony tissue the sarcoma elements soon cause a disappearance of the normal structure, with a rapid resorptive process, the bone melting away, as it were, before the advancing cells of the neoplasm. The bone absorption seems, for the most part, to be the result of the direct action of the tumor cells, although we not infrequently see osteoclasts engaged in a similar process. At the same time an interesting phenomenon may occur, namely, the deposition of new matrix upon the very bone tissue that is undergoing destruction. Such osteoplasia needs careful interpretation since it may either be a normal reactive homeotypical bone proliferation, such as is the rule in syphilis and chronic inflammatory processes, or may be heterotypical or atypical, the result of the activities of bone forming, osteoblastic sarcoma elements. The former type is usually not sufficient in amount to produce architectural changes that need special consideration from the standpoint of diagnosis in the skiagrams; the latter, on the other hand (belonging par excellence to the osteoid, chondroid and true osteosarcomata), is responsible for the striking lime and bone metamorphosis which has already received special mention elsewhere.

By virtue of advance through Haversian canals or by direct extension through places in the *substantia corticalis* that have undergone complete absorption, the neoplasm finds its way under the periosteum. The latter becomes separated from its bony support, first over a small area, and then either by reason of the progress of the tumor, or because of hemorrhages between it and the surface of the bone. It is now that the peculiar phenomenon of new bone formation under and by the periosteum takes place. A study of the skiagrams of gross specimens reveals the interesting fact that the bone deposition occurs in two forms; either as flat stratified lamellæ, disposed parallel with the long axis and surrounding the bone, or, in the shape of fine trabeculæ that have a radiate arrangement, lying perpendicular to the shaft. Both of these varieties can frequently be found in the same specimen. Although my studies of this particular phenomenon cannot be regarded as sufficiently thorough to warrant a decided opinion, it seems to me now that the following explanaton will hold good. The flat lamellæ represent, in part, bony deposits that are the result of bone proliferation from the peripheral layers of corticalis, and, in part, the proliferation that occurs when the periosteum has suffered but minute separation from the bone. Such separation is not confined to the immediate variety of the perforating sarcoma tissue, but extends for a considerable distance up and down the shaft and in a circumferential direction. Thus the first consequence of cortical perforation will be the growth of a thin plate of bone upon the shaft. As the tumor enlarges, a tendency to form a lenticular shaped growth becomes manifest. The periosteal elevation may occur at intervals, depending upon the subperiosteal tension, and each fresh act of separation will be followed by a new accession of lamellar bone growth. Simultaneous with this another modus of periosteal activity is evidenced in the growth of bone trabecula from the periphery toward and perpendicular to the bone. Such radiate disposition is particularly shown in the radiograms and, according to Ribbert, depends on the fact that the perforating vessels have been pulled out in that direction and must, to a certain extent, determine the direction of growth. Be that as it may, we need but note that where the bone covering has suffered any considerable displacement, there the radiate arrangement is purely missed, whereas where the periosteum is separated but a few millimeters or less than a millimeter, the lamellar structure is more apparent.

At the poles of the extraosteal tumor, where the transition between normal and uplifted periosteum must be sought, there a characteristic wedge (in section) or conical shell of bone is regularly seen. The importance of recognizing this structural marking both in diagnosis and in the estimation of the site of origin will receive attention later on.

We have thus far called especial attention to the proliferative phenomena induced by the extraosteal growth. It can readily be appreciated, however, that the new formed periosteal bone will in its turn suffer the same destruction which had already befallen the existing osseous tissue. As a result, the central parts of the cortex of extraosteal spindle will become deprived of its bony covering, a fibrous capsule, the last remnant of periosteum may be left or rupture of this may occur, in consequence of which a rapid growth into the soft parts, or around the periosteum occurs. The periosteum then lies in the tumor mass. This explains the occasional inclusion of periosteum with its adherent bone in parts of extraosteal tumors.

From this description it is evident that, if it is possible to determine the presence of intact periosteum, or to detect evidence of bone proliferation in it, or to trace its dislodgement in the manner suggested, we must be prepared to controvert the opinion that such periosteum contains in it the nucleus of inception of the neoplasm. We must rather seek a focus under the periosteum or in the bone itself.

Of the extraosteal tumors the fusiform type is the ordinary variety. This form may give us—as will be seen later—no indication as to where the beginnings of the tumor lie. Whereas the true spindle, with tapering ends, may be found when the tumor is limited to the shaft, a blunt, and even fungiform overhang may mark its limit at the extremity of a long bone. The absence of the typical periosteal bone wedge may be ascribed to the dense adhesion of the membrane at the epiphyseal region. Besides this we need only mention the nodular, lobules of extraosteal metastases, occasionally seen, and the irregular forms that belong to the stage of periosteal destruction and infiltration of the soft parts.

The Origin of the Bone Sarcomata.

In the light of what has been said we can now better understand the presumptive point of origin of the tumors belonging to our series. Fortified with the knowledge of the rôle played by the periosteum in the development of the bone sarcomata, we must abandon the old conception of division into myelogenous and periosteal varieties. Ribbert recognizes central and peripheral forms. The former originate in most instances in the substantia spongiosa of the diaphysis, although they may grow from any point that lies within the outermost layers of the periosteal bone. Ribbert would have even these so-called peripheral tumors start near one end of the diaphysis and creep up or down the shaft. I shall be able to show that at least this latter view is not in accordance with the data at our disposal.

In establishing the location of the beginnings of the malignant tumors, we must bear in mind a few fundamental facts. A tumor will grow with equal rapidity in all directions, if the resistance offered on all sides is approximately the same. It is just here in the sarcomas of bone that we encounter several difficulties in the proper interpretation of the point at issue. These are the differences of rate of proliferation in bone, and in soft parts, and the limiting powers of the substantia compacta, of the articular cartilage and the periosteum. Thus we cannot offhand place the site of initial growth in the center of the gross product.

Turning to our series, the expansive tumors of the ends of the long bones will be found to arise from a point somewhere in spongy bone of the end of the diaphysis. Beginning, for the most part, in the upper end of the tibia or lower end of the femur, the equal enlargement will leave no doubt as to the correctness of the assumption that they are central in origin.

When we come to consider the expansive tumors of the shaft and the diffuse infiltrating type, we meet with a more intricate problem. Here we may assume a focus either in the marrow, in the innermost layers of the *substantia compacta* or in the spongiosa of the diaphysis. In view of the nature of the histologic types (giant-celled and chondral), it seems most likely that an osseous rather than myelogenous focus is their starting point.

The dissolutive form also arises in all probability in the spongiosa of the diaphysis. The equal destruction of the bone ends is sufficient testimony in favor of this view.

Perhaps none of the tumors afford as much food for investigation as the sclerosing and ossifying sarcomas, when they form fusiform bone encasing spindles, or when they cause that fusion of calcified tumor and bone that makes the identification of a neoplasm so difficult. Here we meet with growths that show both endosteal and extraosteal proliferation. The focus in the bone may be smaller than the mass without. In the interior of the bone there is usually calcification, and often greater in extent than that which forms the petrified core of the extraosteal masses. In these forms the dense nature of the intraosteal focus and the evidences of cortical perforation and the separation of the periosteum leave little doubt that they are endosteal in origin.

Exquisite examples of endosteal origin are given us in the perforative type, in which the central focus is usually much smaller than the extraosteal mass. Here we are not aided in our estimation of the age of the new growth by such a phenomenon as calcification. When we study the relative size of extra- and intraosteal neoplasm and keep in mind the greater rapidity of growth outside of the bone, we shall be forced to find the point of origin within rather than outside of the bone.

Thirty-eight of the forty-six tumors under consideration, therefore, have their inception at points lying either in the spongy bone, in deepest layers of the compacta or possibly in the marrow. My own series (as was already noted in a previous paper)[13] shows but one example of a neoplasm which is not central in origin. At that time our experience did not warrant any decisive conclusions either as to the question of the recognition of periosteal growths or as to the frequency of those that might be classed either as subperiosteal or peripheral. The additional facts gained in the analysis of Rumpel's specimens permit us to take the view that sarcomas do arise from the peripheral layers of the substantia compacta, usually in the shaft; and that Ribbert's assumption of a site of origin in the extremity of the long bones is untenable, at least as far as our own material is concerned. We encounter two types in the eight neoplasms be-

[13] loc. cit.

fore us. In the first there is a subperiosteal tumor without apparent destruction of bone, and in the second the tumor is associated with those osseous changes that are indicative of the neoplasm's destructive growth.

When we find a broad sessile, or fusiform tumor on the shaft, with the signs of periosteal detachment, bone proliferation and cortical erosion, we are led to refer the starting point to the outermost layers of the compacta. In none of the specimens analyzed can we place the point of origin near the extremity of the long bone, and we are forced to the conclusion that the outermost layers of the corticalis should be regarded as the point of origin of the so-called peripheral forms.

Let us review briefly the grouping into seven classes and inquire as to whether these will now stand the test of more careful investigation. Are the points of distinction that permit of this subdivision essential characteristics, are they purely fortuitous, do they depend wholly on the histological variations, or are they in great part but the expressions of differences in situation of the very beginnings of the growths? From what has already been said it is clear that the architecture of the sarcoma and the bone, as we see them, will not be fashioned by any one of these factors, but will show the effects of a combination of several or all. The utility of any grouping, it appears to me, must be estimated especially from the standpoint of value in diagnosis, and of value as an aid in remembering the types. A histological classification is practically useless in this regard.

The expansive types are sufficiently characterized by the absence of tendency to early perforation. The diffusely infiltrating growths may be said to remain confined to the interior of the bone because they arise in the deeper layers of the cortex, in the marrow, or in the middle of the spongiosa. That the site of origin must determine this peculiarity of remaining endosteal to a great extent cannot be denied. However, the late perforation, the slow invasion of the compacta, the extensive intramedullary involvement, the striking difference between the development here and in the dissolutive and perforative types, these facts warrant making a separate class of these forms. The fourth group —the dissolutive type—presents a marked contrast to the expansive type and merits, therefore, the special consideration which it has received. It might be urged that, were this type to owe its inception to a focus near the cortex, the perforative endosteal variety might result. We must grant this to be the case, and that this criticism is not a negligible one. We need hardly pause to discuss the utility of recognizing the sclerosing type; for the diagnostic points brought out by a study of the pathology of these tumors have been dwelt upon elsewhere. As regards the perforative endosteal tumors, can the gross structural changes be explained altogether by the assumption that here, too, the initial process is nearer the periphery than the center of the bone? It seems that a difference in site of origin cannot be the only factor. For is it not striking that in the case of certain varieties (the diffusely infiltrating—and expansive), a marked resistance is offered by the cortical shell, whereas just here early penetration occurs? It would be possible to explain the configuration of these tumors only by supposing a beginning in the cortex itself. The relative size of extra and intraosteal masses will not permit of such an hypothesis in all cases. In those instances in which an extraosteal tumor is not very much larger than the endosteal mass the growth could hardly start so near the periphery, for the progress without must be much more rapid than within the bone. All in all, it seems best at this juncture to call attention to this variety by means of special grouping, leaving the final adjudication of the admissibilty of such grouping until more specimens shall have come under observation.

Finally, a word as to the peripheral forms. Ribbert includes here all those sarcomas that originate in bone of periosteal origin. Inasmuch as it becomes practically impossible to decide the exact point of origin from the study of the specimens, and a certain latitude of error must be allowed, such a basis for distinguishing the peripheral varieties seems inadequate. From a consideration of my own material and the study of the available data given by Rumpel, it would be best to include in the peripheral class only those neoplasms which show either subperiosteal growth without change in the bone, or subperiosteal growth with those typical erosive lesions that indicate to us a genesis in the most superficial layers of the cortex.

Discussion.

DR. JAMES EWING, after expressing his admiration for Dr. Buerger's careful work, asked him whether it was not possible that some of the seven varieties which he had described might be representative of different stages of the same process, and further whether a close study of the histology of the tumors might not furnish evidence which would enable him to group together and perhaps reduce the number of the classes.

DR. CHARLES NORRIS asked how Dr. Buerger was able to determine the older portions of the growth, of which he had spoken several times.

DR. BUERGER said, in regard to Dr. Ewing's query as to whether some of these classes might not represent various stages of the same process, that he must admit that he had himself made the same criticism. Time had prevented him from going into this matter minutely. Briefly, however, it might be said that expansive tumors were, of course, sufficiently characteristic; they certainly differed materially from the rest. The same could be said of the sclerosing type. The only trouble would arise in differentiating the diffusely infiltrating variety, the destructive variety, and the perforative type. As regards the perforative endosteal tumors, can the gross structural changes be explained altogether by the assumption that here, too, the initial process is nearer the periphery than the center of the bone? It seems that a difference in site of origin can not be the only factor. For is it not striking that, in the case of certain varieties (the diffusely infiltrating and expansive), a marked resistance is offered by the cortical shell, whereas just here early penetration occurs? It would be possible to explain the configuration of these tumors only by assuming a beginning in the cortex itself. The relative size of extra- and intraosteal masses will not permit of such an hypothesis in all cases. As to the other two: the destructive forms are characterized by early destruction of the cortex, which is in marked contrast to the infiltrating forms. This peculiarity and their intense dissolutive powers permit of placing them in a class by themselves. As to whether something more could not be learned from a study of the histology of these tumors, in the way of correlating histological and gross types, Dr. Buerger said that he had not had much success except in the osteoid and chondroid forms where there is the intense calcification and bone formation. The other forms could not be associated with histological changes. In regard to the possibility of distinguishing the older portions of the tumors, Dr. Buerger said that this could be done only in the osteoid tumors where the oldest portions were accompanied by the greatest amount of calcification, whereas the younger parts were soft.

FILARIA IN SECTIONS OF INGUINAL LYMPH NODE.

B. C. CROWELL, M.D.

The case for presentation refers to a native of the Danish West Indies, thirty-two years of age, who was admitted to the hospital service of Dr. Hayden for a swelling in the right groin, which he had had since a boy. He has been in this country six years. This swelling has been treated by cupping a few times with temporary improvement, and at one time, it was opened and a small amount of blood expressed. He had large femoral and inguinal nodes on the right side, over which there was considerable edema. His right epididymis was enlarged, hardened, and nodular. There was some thickening of the right spermatic cord and evidence of moderate left-sided hydrocele. A few of the very large inguinal nodes were removed for diagnosis. On routine section of these, which showed a chronic hypeprlastic lymphadenitis, there was discovered in a very much thickened and dilated lymphatic a section of what is apparently a nematode worm which corresponds to the descriptions of *Filaria Bancrofti* coiled on itself. It consists of a musculo-cutaneous margin enclosing a thin-walled bilobed uterus and an alimentary canal whose walls are pigmented. The uterus contains numerous ova and embryo filariæ, some of which can be seen outside of the parent worm in the lymphatic space. The lymphatics show very well the characteristic connective tissue and muscular thickening. Further examination of the patient was not made, aside from a single afternoon blood examination which showed no leucocytosis and 8.5 per cent. of eosinophiles.

Very few cases of such findings have been recorded. In 1900 Lothrop and Pratt reported finding of worms in the epididymis; and in 1901 Opie also found worms in the epididymis associated with an immense lymphatic varix involving the thoracic duct and all of the retroperitoneal lymphatics and extending into the scrotum. One other case of accidental finding of the parent worm in the hardened tissues was previously reported. Dr. James Ewing said that he had had a similar case at the Cornell Medical College six years ago.

EXTENSIVE THROMBOSIS OF THE CERVICAL VEINS FOLLOWING (a) ACUTE AND (b) CHRONIC OTITIS MEDIA.

B. C. CROWELL, M.D., AND A. B. EISENBREY, M.D.

(a) We are enabled to report the following case through the courtesy of Dr. H. M. Taylor.

B. L. I., male, aged twelve years, during convalescence from an attack of measles of average severity, developed a high irregular temperature with symptoms referable to a right-sided otitis media with mastoid infection. When the condition had continued for five days, operation was decided upon. It was found that the external jugular vein on the right side was thrombosed and that abscesses were present in the right hand and right ankle. In addition to the mastoidectomy and opening of the right lateral sinus, phlebectomy was performed and the abscesses were drained. After operation there was temporary remission of the acute symptoms, followed by recurrence and death on the fourth day.

Autopsy.—Cause of death: Septicæmia (streptococcus); otitis media, acute suppurative, right side; thrombosis of lateral and petrosal sinuses, right side; thrombosis of cervical veins; pericarditis, fibrino-purulent; endocarditis, acute mural and valvular; acute parenchymatous degeneration and abscess of heart muscle; bronchopneumonia, terminal; acute splenic tumor; acute parenchymatous degeneration of liver; acute parenchymatous degeneration of kidneys; abscess of right hand, right ankle, and left gluteal region.

Smears from pus of middle ear showed numerous streptococci and a few staphylococci. Smears from lung showed a few streptococci, numerous pneumococci and large numbers of staphylococci. Culture of blood from heart showed a pure growth of streptococci.

The brain, with the exception of a small area of softening directly beneath the operative field, where the anterior margin of the right side of the cerebellum lay in contact with the lateral sinus, showed no macroscopic lesions further than a general congestion of the pial vessels. The cerebrospinal fluid was clear. No thrombosis of the cerebral vessels or abscess formation was found.

The longitudinal sinus contained considerable fluid blood and a small chicken fat clot. On the left side of the cranial cavity all of the sinuses were free and contained fluid blood. On the right side the lateral sinus contained a firm thrombus extending from the point where it had been opened into backward to the torcula, and anteriorly both petrosal sinuses were thrombosed. The middle ear on the right side was the seat of an acute suppurative process which had extended backward into the cancellous bone. On the left side the middle ear appeared normal.

The heart contained fluid blood and in the right ventricle a small chicken fat clot was present. No thrombosis of the pulmonary vessels or infarction of the lungs was found. After removal of the heart, the superior vena cava was examined and found to contain a firm mass which, when grasped by forceps, was readily removed and revealed a thrombotic cast of the cervical veins. Unfortunately the early removal of the mass made it impossible to ascertain just which of the cervical veins were involved in the process, and dissection of the neck which might have revealed further evidences of thrombosis of the vessels was not undertaken.

The specimen presented consists of the cast of the cervical veins made up of the thrombus which was removed as previously described. Its appearance indicates that the process was more extensive and that, in removal, parts of it were broken off and remained in other branches of the vessels.

(b) The case for presentation is that of an Irish woman, forty-five years of age, who about four years ago was said to have had an attack of meningitis, since which she had had marked loss of memory and had complained of her right ear, saying that it "felt as though stuffed up." At no time was deafness or a discharge noticed. She also had extensive ulcerations on the leg, which had been skin grafted. Her admission to the hospital was on account of her leg condition and while in the hospital she was regarded as a case of endocarditis, on account of the irregularity of the heart and the presence of a systolic murmur over the precordium.

At autopsy she was found to have an extensive thrombosis, involving the entire superior vena cava, both innominate, external and internal jugular veins, the right lateral sinus, and the temporo-sphenoidal and occipital veins. She had a chronic right-sided otitis media and mastoiditis; there was no cerebral or meningeal congestion or edema. The other lesions present were slight parenchymatous and chronic interstitial nephritis; double hydrothorax and nutmeg liver. The thrombi were old, definitely adherent, mixed thrombi, firmer and paler in the portions near the heart than in the cranial vessels.

Cultures made from the spleen and innominate veins show small curved and clubbed Gram positive rods, resembling pseudodiphtheria bacilli, but the relation of these organisms to the thrombosis was not determinable. Microscopical section of the innominate vein with thrombus shows an extensive chronic phlebitis, with loss of the endothelium at the point where the thrombus was attached, breaking up of the internal elastic layer and a considerable disintegration of the media with thickening and thrombosis in the adventitia.

A CASE OF CHRONIC OR UNRESOLVED PNEUMONIA, POLYSEROSITIS, AND SENILE MALNUTRITION.

JAMES EWING, M.D.

The term unresolved pneumonia is not always applied to the same condition. By some it is used to designate a type of pneumonia in which the exudate consists chiefly of a homogenous fibrinoid material very poor in leucocytes, which is followed by organization of the exudate by spindle cells, proliferation in the walls of air vesicles, fusion of plugs of exudate, and gradual contraction of the involved pulmonary lobe into scar tissue. More often the patient dies in the acute stage of this pneumonia, and cicatrization never occurs. Several years ago Delafield showed that this type of pneumonia is a specific variety and is not merely a failure of resolution of an ordinary lobar pneumonia. Slightly delayed resolution of an ordinary pneumonic exudate is probably not an uncommon event, but persistent failure of resolution in a lobar pneumonia extending over many weeks, and even many months, is extremely rare, so that the present case illustrating persistence of an ordinary lobar pneumonia for about fourteen months seems to be worth recording.

The patient was a man, sixty-one years of age, who had suffered for several years from indigestion and malnutrition which reached such a grade that he eventually became extremely emaciated. No definite cause of this trouble could be discovered by various specialists here and abroad. During 1908 the vision in the right eye became impaired, and in July, 1908, this eye was removed for a condition which some regarded as syphilis. The ocular lesions consisted in a productive round cell inflammation of much of the choroid with detachment of the retina.

In November, 1908, he was taken acutely ill with fever and signs of consolidation of the right lung. These signs and symptoms continued irregularly until his death in January, 1910. During this period of about fourteen months he was seldom free from fever and dyspnea, and was confined to bed. For many weeks he received pneumococcus vaccines. After the subsidence of the acute symptoms the attention of his physician was drawn away from the pulmonary condition to his progressive emaciation which reached an extreme degree, the body finally consisting chiefly of skin, bones, and extremely thin ribbon-like muscles. There were arthritic symptoms, pains, loss of reflexes, and ataxia, which suggested tabes. The Wassermann test was negative. The urine was free from albumin and gave no indication of renal disease. The heart's action was accelerated and weak. There were constant moderate dyspnea and numerous attacks of severe dyspnea which the patient could be induced to overcome by voluntary efforts at respiration. There was no hypertension. The feeding of the patient was accomplished with great difficulty, as he would eat little of anything. Ingestion of meat or eggs was sometimes followed by severe indigestion and intoxication, so that this form of diet had eventually to be omitted altogether and he was given small quantities of fruit and cereals. During the last three months there was little fever. During the last month there were several syncopal attacks with dyspnea in one of which he finally died.

The anatomical diagnosis at autopsy was as follows:

Partial pneumonic consolidation of right lower and posterior portions of upper lobe. Extensive chronic fibrinous pleurisy over both lungs, especially the right, with slight serous exudate over right. Universal adhesive pericarditis. Chronic mediastinitis. Chronic perihepatitis binding upper surface of liver to diaphragm. Chronic perisplenitis causing constriction of colon. Dilatation of stomach with atrophy of gastric mucosa. Advanced chronic diffuse nephritis of right kidney. Nearly complete atrophy of left kidney. Extensive hyperplasia of adrenals. Marked atrophy of pancreas with preservation of islands of Langerhans. Marked sclerosis and atrophy of thyroid.

Microscopical Examination.

The consolidated portions of the lung show an exudate filling the air vesicles, composed of globules and strands of loose fibrin, polynuclear leucocytes, exfoliated epithelium, and serous fluid. The walls of the vesicles are, in places, thickened by many spindle cells, and the capillaries are deficient. Some vesicles are partly obliterated by the thickened walls. In other places the vesicles are dilated and filled with exudate. There is no organization of the exudate. The walls of bronchioles are edematous and infiltrated with a few round cells. The pleura is much thickened by a layer of granulation tissue which extends well into the fibrinous exudate. Sections of the pericardium present the same appearance. Gram's stain shows many encapsulated diplococci in the pleura and a few throughout the lung.

There was, therefore, a condition of chronic unresolved pneumonia, due probably to pneumococcus infection. The inflammation extended slightly to the other lung, to the pericardium, mediastinum, under surface of diaphragm, and slightly to the spleen. The dyspnea was fully explained by the persistent pneumonia and pleurisy, and especially by the pericarditis, and the feeble circulation was evidenced by the well-marked changes of chronic congestion of the liver.

The emaciation and failure of nutrition antedated the pneumonia and must be referred to other factors. The extensive renal lesions failed to yield any of the urinary, circulatory, or toxic signs of Bright's disease, but there may be found reasons for supposing that they contributed essentially to the general failure of nutrition. Other factors leading to the same result are found in the stomach and thyroid gland. The gastric mucosa was everywhere reduced to about one-half its normal thickness, the peptic glands were represented by very short tubes very deficient in acid cells, and the muscularis was unusually thin. There was very little new connective tissue in the mucosa. Little attention is commonly paid to the atrophic thyroid often found in elderly subjects, but it is clear that an extremely fibrous and atrophic thyroid must signify deficient capacity to metabolize nitrogenous food, a defect which was very notable in this patient. The parathyroids were also atrophic and its cells resembled small lymphocytes. The atrophy of the kidneys may perhaps be correlated with the atrophic thyroid and both together with the gastric atrophy may account for the emaciation and failure to maintain the nutrition of protein tissues.

A curious relation existed between the adrenal and pancreas which is of interest in connection with the theories regarding the metabolic functions of these organs. The adrenals were enormously hypertrophied, measuring 7 x 4 x 1.5 cm., and contained a corresponding excess of chromaffine cells. One may suppose that this condition indicated an unusual capacity to metabolize carbohydrates. In the pancreas there was extensive reduction of alveoli devoted to external secretion, while the islands of Langerhans were increased in number and size. This condition may indicate increased capacity to burn carbohydrates. As a matter of fact, during the last two years the patient lived chiefly on carbohydrates and showed a marked repugnance toward meats.

In a patient whose failing nutrition seems to have depended on such marked changes in stomach, kidneys, thyroid, pancreas, and adrenals it is perhaps not a matter of surprise that a complicating pneumonia should fail to resolve, especially if, as it is said, immunity is ultimately a function of the organs.

A diagnosis of syphilis was made by several of the many consultants in this case. Aside from the ocular lesion, which failed to show spirochetes or the definite histological signs of syphilis, there were none of the organic lesions upon which one depends for the anatomical diagnosis of late syphilis. Levaditi stains of many tissues were all negative.

It has long been known that many cases of adhesive pericarditis and mediastinitis are associated with chronic pleurisy and followed by chronic peritonitis, swelling of the liver, and ascites, constituting a condition often called polyserositis. This condition has been described especially by Romberg,[1] Pick,[2] Hess,[3] and others, but the exact etiology and pathogenesis of the condition have not been made clear. Recently Schlayer,[4] in Romberg's clinic, has expressed the opinion that the disease is essentially an inflammatory process which extends from pleura, pericardium, and mediastinum to the liver and peritoneum, and that stasis from heart weakness has little to do with the severe inflammations and exudates. The present case resembles some of those reported by Schlayer, and since in this instance the etiology and course of events starting from the pneumonia are quite clear the observations may have some bearing on the nature of more chronic and typical cases of Romberg's disease in which the relation to previous acute pleurisy or pneumonia is not apparent.

REFERENCES.

[1] ROMBERG: Lehrb. d. Krankh. d. Herzens u. d. Gefässe.
[2] PICK: *Ztschr. f. klin. Med.*, 1896, xxix, 385.
[3] HESS: Uber Stauung. u. chron. Entzund. in d. Leber. Marburg, 1902.
[4] SCHLAYER: *München. med. Wchnschr.*, 1910, lvii, 729.

Discussion.

DR. CHARLES NORRIS asked where the unresolved pneumonia was—in the upper or lower lobe. He had understood Dr.

Ewing to say that the patient had had an adhesive pericarditis. Was this really a lung in which the formation of connective tissue took place?

Dr. Richard M. Pearce had understood that there was really no organizing pneumonia in the lung. There was simply the history of pneumonia without resolution. He asked whether it was justifiable to assume that an acute inflammatory condition was constantly present in the lung during the entire fourteen months. Might it not be possible that the individual had had recurrent attacks of pneumonia?

Dr. W. G. MacCallum asked whether there was any record of the patient's blood pressure.

Dr. Ewing said that the location of the pneumonia was chiefly in the right lower lobe; to some extent in the upper; the other lung was slightly affected. The pericarditis was dry with contraction, and the heart was small, so that there was no pressure on the heart. Regarding the identity of the condition found at autopsy with that giving the acute symptoms in the beginning of the illness, it was concluded that the condition of the lungs at death was representative of and the direct result of the condition established at the time of the acute attack, principally on account of the clinical history, which showed continuation of the auscultatory signs at the exact point of attack. An exacerbation might have occurred just before death, but was strongly contraindicated by the history. There was nothing in the clinical history to indicate a terminal pneumonia. There was no organization of the exudate. There was some thickening of the walls of the vesicles which would be likely to accompany a prolonged process of this sort. There were no determinations of the patient's blood pressure. The pulse was not of high tension, and there was not the slightest suspicion that the patient has such extensive disease of the kidneys. There was very slight arteriosclerosis.

Dr. Norris suggested the possibility that this might be a case of aspiration pneumonia. He questioned the possibility of an acute pneumonia lasting for fourteen months.

Dr. Ewing thought that Dr. Norris would agree, after he had examined the specimens and the sections under the microscope, that there was not the slightest ground for the suggestion of aspiration pneumonia. He would repeat that the patient had been a source of great interest to many prominent clinicians for a long period. There was nothing lacking in the clinical observation, and he was, therefore, able to offer these clinical data with some assurance.

Dr. Norris thought that most of the aspiration pneumonias were never diagnosed by the clinicians, and that many cases of Bright's disease were also not diagnosed during life.

THE BACILLUS OF RHINOSCLEROMA.

WILLIAM C. THRO, M.D.

The organism here described was obtained from an individual under the care of Dr. C. G. Coakley. The histological diagnosis of rhinoscleroma was made by Dr. W. J. Elser, who suggested that the organism be studied and that treatment by vaccination might be beneficial.

Clinical History.—The patient, a Russian, thirty-five years of age, male, has lived in the United States for fifteen years. The nodal lesion was first discovered four years ago by a surgeon who was treating him for deafness. At the present time it is confined to the nose, which is slightly enlarged externally, with partial occlusion of the left nares and almost entire obliteration of the right.

Sections from the mass show the characteristic structure of rhinoscleroma, and in the hyaline areas the encapsulated bacilli, supposed to be the etiological factor, were found.

From a study of the literature it is evident that there are different strains of the bacillus of rhinoscleroma. For example, Paltauf states that it coagulates milk; Abel that it does not.

Some strains produce gas with saccharose, and others do not. The strain isolated from this case grows in cultures as diplococci, or short or long rods, singly or in chains. The organism has a large, well-developed capsule similar to *B. mucosus capsulatus*. It is non-motile and Gram-negative. At 37° C. it grows luxuriantly in all the media tested and it lives for months at room temperature.

The growth in various media will be compared with that of three strains of *B. mucosus capsulatus,* one from an abscess, designated "Elser"; one from a case of pneumonia, designated "Shea"; and one from a case of chronic bronchitis, designated "Guide."

Broth.—All three organisms clouded the broth uniformly, with the formation of a ring at the surface of the media, and an abundant white sediment. The bacillus of rhinoscleroma occurred in broth in long chains of encapsulated rods.

Agar.—On the original plates (isolated December 18, 1909) the surface colonies of *B. rhinoscleromatis* were 1 millimeter in diameter after twenty-two hours, whitish, opaque, and circular, with irregular edges. The deep colonies were similar except that they were more transparent and died out sooner. When touched with a loop the growth could be drawn out to a distance of 1 cm., which is a well-known characteristic of *B. mucosus capsulatus.* On slant agar, the growth is abundant, thick, shiny, spreading, and whitish.

Milk.—*B. rhinoscleromatis* and two strains of *B. mucosus capsulatus* did not coagulate the milk, while one strain of the latter did.

Potato.—On potato *B. rhinoscleromatis* grew very sparsely, and in this respect differed from the strains of *B. mucosus capsulatus* which produced an abundant growth in twenty-four hours resembling, on the upper portion of the potato, clumps of small white beads.

Dunham's Peptone Solution.—*B. rhinoscleromatis* and all the strains of *B. mucosus capsulatus* produced a slight cloudiness of the peptone solution, and all gave a faint indol reaction.

Hiss' Serum Inulin.—None of the strains coagulated this medium at the end of five days.

Gelatin.—None of the strains liquefied gelatin. At the end of twenty-four hours *B. rhinoscleromatis* had grown only one-half the length of the stab, but ultimately it grew the full length, as did also the strains of *B. mucosus capsulatus.*

Carbohydrates.—The sugar-free agar and broth were made up according to directions given by Elser and Huntoon.[1] Merck's dextrose, levulose, saccharose, lactose, maltose, mannit, galactose, dextrin, inulin, and dulcite were used. In inoculating the agar the straight wire was drawn along the slant and the medium was then stabbed. At the end of twenty-four hours *B. rhinoscleromatis* caused a faintly acid reaction in the agar containing dextrose, levulose, mannit, and galactose, and at the end of forty-eight hours the maltose medium was also acid. At the end of several weeks an acid reaction was obtained with all the carbohydrates except lactose, dextrin, inulin, and dulcite, which were alkaline. With mannit and inulin the lower portion of the agar ultimately became decolorized. The reaction of the different strains and the changes taking place are shown in the table.

In the fermentation tubes *B. rhinoscleromatis* never produced gas by the end of thirty days. The closed arm became clouded with all except lactose, dextrose, and dulcite media.

None of the strains of *B. mucosus capsulatus* produced gas in inulin, dulcite, or dextrin media. One, however, produced gas in the other media, though very slowly in saccharose. Another strain differed from the preceding in the non-production of gas in lactose, while a third strain of *B. mucosus capsulatus* did not produce gas in lactose and produced only a bubble of gas in saccharose and maltose. The reaction of the media in the bulbs changed from day to day.

Agglutination.—The chief object in isolating the organism from this patient was to try the effect of vaccine therapy. Before the first injection of vaccine the patient's serum was tested

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[1] Elser and Huntoon: Studies on Meningitis, *Jour. Med. Research*, 1909, xx, 375.

TABLE I.—CULTURAL CHARACTERS

NAME OF CULTURE	BROTH	MILK	GELATIN	POTATO	HISS' SERUM INULIN	INDOL DUNHAM'S PEPTONE
B. rhinoscleromatis	Cloudy Much sediment	Not coagulated	Not liquified Nail-like	Slight growth	Not coagulated	Faint trace
B. mucosus capsulatus "ELSER"	Uniformly cloudy Distinct ring at top of media	Coagulated	Not liquified Nail-like	Good growth Raised, pale, yellow, shiny	Not coagulated	Faint trace
B. mucosus capsulatus "SHEA"	Uniformly cloudy Ring at top of media	Not coagulated	Not liquified Nail-like	Good growth Raised, shiny, granular	Not coagulated	Faint trace
B. mucosus capsulatus "GUIDE"	Uniformly cloudy Ring at top of media	Not coagulated	Not liquified	Good growth Raised, shiny, granular	Not coagulated	Faint trace

Table II.—CARBOHYDRATE

Name of Culture	Dextrose			Levulose			Saccharose			Lactose		
	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm
B. rhinoscleromatis	0	Ac	+	0	Ac	+	0	Ac	+	0	Alk	0
B. mucosus capsulatus "Elser"	.66	Ac	+	.56	Alk	+	.35	Alk	+	.58	Ac	+
B. mucosus capsulatus "Shea"	.50	3d Ac	+	.70	3d Alk	+	.25	3d Alk	+	0	3d Alk	0
B. mucosus capsulatus "Guide,'	.13	Ac	+	.13	Ac	+	.01	Ac	+	0	Alk	+

CARBOHYDRATES

Name of Culture	Dextrose			Levulose			Saccharose			Lactose		
	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days
B. rhinoscleromatis	Ac	R	R	Ac	R	R	N	B R	B R	N	B	B
B. mucosus capsulatus "Elser"	Ac	R Y	R	Ac	R	R	Ac	B R Y	B Y	Ac	R Y	R Y
B. mucosus capsulatus "Shea"	Ac	B Y	B Y	Ac	R Y	B Y	Ac	B Y	B Y	Alk	B Y N	B Y
B. mucosus capsulatus "Guide"	Ac	R Y	R	Ac	R	R	Ac	R Y R	R	Ac	R Y R	R

Ac—*Acid.* Alk—*Alkaline.* N—*Neutral.* R—*Red.* Y—*Yellow*

The decimals refer to the proportion of the closed arm filled with gas.

N FERMENTATION TUBES

LTOSE		MANNIT			GALACTOSE			DEXTRIN			INULIN			DULCITE		
Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm
Ac	+	0	Ac	+	0	Ac	+	0	Alk	0	0	Alk	+	0	Alk	
Ac	+	.83	Alk	+	.71	Ac	+	0	Alk	+	0	Alk	+	0		+
3d lk	+	.35	3d Ac	+	.50	3d Ac	+	0	3d Alk	+	0	3d Alk	+	0	3d Alk	0
Ac	+	.52	Ac	+	.25	Ac	+	0	Alk	0	0	Alk	+	0	Alk	0

LITMUS AGAR

LTOSE		MANNIT			GALACTOSE			DEXTRIN			INULIN			DULCITE		
Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days
R	R	Ac	B Y	B	Ac	R	B R	N	B	B	N	B Y	B Y	N	B N	B N
R Y	R Y	Ac	B Y	B Y	Ac	R Y	R Y	Ac	B Y	B Y	N	B Y	B Y	N	B	B
B Y N	B Y	Ac	B Y	B Y	Ac	B Y	B Y	Alk	B Y R	B Y	Alk	B Y N	B Y	Alk	B N	B
R Y R	R	Ac	R Y	B Y	Ac	R Y R	R Y	Alk	B Y N	B Y	Alk	B Y	B	Alk	B N	B Y

B—*Blue or Alkaline.*

for agglutinins in dilutions varying from 1 to 10 to 1 to 50. The results were negative. After treatment for one month the serum was again tested with similar results.

Treatment.—The bacteria used for vaccination were heated at 65° to 70° C. for one hour. All the injections were given subcutaneously in the arm. The patient was weighed frequently, and there was no great variation. After some injections there were slight redness and pain at the site of the injection, and several times the patient had attacks of epistaxis and tenderness of the nose on pressure.

The results are negative, since there has been no change in the size of the growth, although the patient states that he can breathe much more easily.

The dosage of the vaccines was as follows:

Jan. 11.— 15 millions.
" 15.— 20 "
" 18.— 25 "
" 22.— 35 "
" 25.— 45 "
" 29.— 45 "
Feb. 8.— 60 "
" 15.— 60 "
" 19.— 65 "
" 22.— 65 "
" 26.— 75 "
Mar. 1.—105 "
" 5.— 97 "
" 8.— 97 "
" 12.—112 "

Mar. 19.—132 millions.
" 22.—144 "
" 26.—165 "
" 29.—198 "
Apr. 2.—264 "
" 5.—330 "
" 12.—528 "
" 19.—594 "
" 26.—574 "
May 2.—528 "
" 12.—600 "
" 19.—637 "
" 24.—637 "
" 31.—637 "

I wish to thank Dr. W. J. Elser and Dr. R. M. Pearce for aid and suggestions in the preparation of this paper.

Discussion.

Dr. F. S. Mandlebaum had had the good fortune to examine material from four cases of rhinoscleroma. The first two cases were typical ones and occurred some ten or twelve years ago. Four years ago a young woman of sixteen had presented herself at the out-patient department of Mt. Sinai Hospital with a lesion of the larynx and trachea. A small portion of the larynx was excised and sent to the laboratory for diagnosis. Remembering the picture of the slides in the earlier cases, Dr. Mandlebaum was able to make a diagnosis of scleroma. This case was the first in this country of primary scleroma of the trachea and pharynx. The Mikulicz' bodies were found in great profusion and the smaller ones were filled with the bacilli. The larger cells showed the bacilli scattered at the periphery, and this was apparently caused by a mucoid degeneration or some product of secretion from the capsules of these organisms. These cells and their bacilli stained with the ordinary basic anilin dyes as well as with hematoxylin, and could be readily seen. The hyalin bodies showed some rather peculiar features; they formed distinct rosettes with a sort of nuclear substance usually found in the central portion; and they were very symmetrical. At times some of the hyalin material did not stain well. The Gram stain proved to be the best for bringing out the hyalin body, but it also stained well with acid stains, such as eosin or picric acid. Dr. Mandlebaum showed photomicrographs made at the time he had studied the case, one of low power showing the Mikulicz' cells rather well filled with bacilli. The higher power, 1000 diameters, showed one of the large cells in which the bacilli were seen only at the periphery. Occasionally some bacilli were seen in the tissues about the cells. Other photographs were made simply to show the hyalin body present in large numbers and the rosette forms. The first sections were stained with polychrome methylene blue which seemed to be the very best of all staining agents for the purpose. Cultures were made from this case; and an organism was grown which was practically identical with Friedländer's bacillus.

ADENOMYOMA OF THE FALLOPIAN TUBE.

W. G. MAC CALLUM, M.D.

The case was one operated upon at the German Hospital by Dr. Seeligman for the extirpation of a myomatous uterus in which enlargements of the Fallopian tubes were found as an accidental discovery. On one side there was a small nodule situated about one centimeter from the cornu of the uterus—on the other side the proximal part of the tube was of normal size, while an enlargement of considerable size occupied the middle portion extending toward the fimbriated extremity. This mass measured 25 cm. in diameter and was irregular and nodular in form. Transverse sections through the small nodule on the left side showed several lumina. On the right side accessory lumina appeared in the apparently normal portion of the tube between the cornu and the large nodule. Section through the nodule itself revealed a number of cyst-like cavities filled with a brown turbid fluid. These are seen to be lined with a cubical or columnar epithelium and to be associated with numerous microscopic masses of gland-like or tubular spaces lined with similar epithelium and quite separate from whatever may represent the original lumen of the tube. In association with these new formations there is a great excess of smooth muscle tissue.

It seems clear that this is an example of the adenomyoma of the Fallopian tube, such as has been described by von Recklinghausen, Emil Ries and others.

Von Recklinghausen explained their origin by considering them the result of the development of remnants of the Wolffian duct which runs in intimate relation with the uterus, crossing the Fallopian tube near the cornu, while others, such as Ries and Cullen, think it more probable that the epithelial lined cavities arise from the epithelium of the mucosa of the tube or of the uterus, either as a result of displacement or as the remote effect of distorting inflammatory processes.

In this instance there is no evidence of even the remnants of an inflammatory process and the case was, therefore, regarded as a true adenomyoma developing in the tube.

In spite of the counter evidence there still seems to be much to be said in favor of von Recklinghausen's theory.

AN UNUSUAL LESION OF THE LARGE INTESTINE.

S. R. BLATTEIS, M.D.

History.—D. J., aged thirty-four, admitted to the Jewish Hospital, of Brooklyn, in the service of Dr. William Linder on April 5, 1910, a native of Warsaw, Russia. Family history negative. Patient had the usual diseases of childhood; has been six years in this country; is a tailor by occupation; is married and has had five children, three of whom are living; one died of diphtheria, the other of measles. He smokes and drinks moderately; denies venereal disease. Never had a doctor since childhood until December 15, 1909, when, while in apparent good health, he was seized with severe abdominal cramps which lasted intermittently through the night and the following morning. His case was then diagnosed as appendicitis, and operation was advised. As his condition somewhat improved, this was refused.

From that time until the time of operation, April 15, 1910 (four months), the patient suffered from numerous attacks of abdominal pain that were distinctly referable to the right iliac fossa. From the first attack until the day of operation he suffered from attacks of indigestion and a great deal of flatulence, complaining of annoying gurglings in the right iliac fossa. His appetite was fair; he never vomited, was very constipated, gradually failed in health and became thinner and very anemic.

The urine and feces were normal. The blood count on April 6, nine days before the operation, was as follows: Total leucocytes, 11,200; polymorphonuclears, 68 per cent.; small and large lymphocytes, 28 per cent.; mononuclears and transitionals, 3.5 per cent.; eosinophiles, 0.5 per cent. For nine days before the operation his temperature varied from 98.6° to 100.6°. An *x*-ray examination showed nothing. The Wassermann reaction was negative.

The post-operative history can be summed up in the statement that "the patient is making an uneventful recovery." All the pain has disappeared and his bowels have a normal daily evacuation.

Gross Description of Specimen.—The resected intestine measures 37 cm. and consists of 5 cm. of the ileum, the appendix, the cecum, the ascending colon, and the beginning of the transverse colon. With the exception of 6 cm. of the end of the transverse portion, the specimen shows the following:

The wall of the intestine is markedly thickened and edematous, varying in thickness from 1.5 cm. at the cecum to 2 cm. at some portions of the ascending colon, the thinnest portion being from 3 to 5 mm. This thickening is confined almost exclusively to the submucosa, there being but slight thickening of the muscularis.

Macroscopically, the submucosa appears to be honeycombed, very strongly resembling tissue after infection with the *B. aerogenes capsulatus;* these cystic chambers vary in size from 1 to 3 mm. in diameter and are irregular in shape. As a result of this swelling of the intestinal wall, the mucous membrane is thrown into numerous thick folds; there are also evidences of varying degrees of inflammation. The mucous membrane is covered with a thick tenacious mucus.

The appendix is 6 cm. long, is of the usual thickness, and does not show the changes described in the intestine. Attached to the intestine is the greater part of the ascending mesocolon. Along the mesentery of the ileo-cecal portion are a number of enlarged lymph nodes varying in size from 0.5 to 1 cm. on cross section. These glands, except for their size, show no abnormal appearance.

Three pieces of the intestine were submitted for examination, one from the central portion, and one from each end of the resected intestine.

Pathological Examination.—Intestine.—The lesions are essentially alike in all portions of the specimen. The characteristic lesion is in the submucous coat and consists in the extreme dilatation of the lymphatic vessels, in consequence of which this coat is much swollen and presents to the naked eye a honey-combed appearance, due to the presence of numerous cystic spaces, with intervening, often thin septa of connective tissue. These spaces are present throughout the submucosa, but tend to be rather larger and closer together in the internal part than in the part near the muscular coat.

While there is a uniform swelling of the submucosa, this swelling is greater in some places, so that these project further toward the lumen of the intestine. The cysts vary in size and shape; some are round or oval; others are irregular in shape, with thin septa crossing them or extending only into their lumina. There are evidences of the coalescence of the cystic spaces by atrophy of the adjacent septa. Many of the cavities are empty; others contain a finely granular material; still others contain fibrin and leucocytes or masses of leucocytes. Most of the cavities are lined with a single layer of endothelium; some are lined with several layers of proliferating endothelium.

The leucocytes within the dilated lymphatics are of both the polynuclear and the lymphocytic types, including plasma cells and also eosinophiles. Polymorphonuclear leucocytes are numerous, many of these being eosinophilic. A conspicuous feature of the lesion is the presence within the dilated spaces of large numbers of giant cells with central multiple nuclei. In some instances these almost completely fill up the spaces, and in others are arranged so as to form their inner lining. These cells, in the main, resemble foreign body giant cells.

The intervening stroma is connective tissue which in a few places is densely fibrous, but in most places is edematous and richly infiltrated with cells. Proliferating connective tissue cells are seen, but the predominant cells in the meshes of the edematous tissue are leucocytes, both mononuclear and polynuclear, and not infrequently eosinophilic. There are places, especially near the muscularis mucosæ, where the leucocytes are densely packed and are undergoing necrosis with extensive nuclear fragmentation. Delicately fibrillated fibrin is abundant, although not uniformly present in the meshes of the connective tissue of the submucous coat. The solitary follicles appear essentially normal, perhaps in some instances moderately swollen. The mucous membrane is intact. The cells of Lieberkühn's glands are well preserved and are mostly calyciform. The lymphatic tissue of the mucosa appears essentially normal. The lymphatics of the mucosa, if dilated at all, are only moderately so, and do not show cystic dilatation as in the submucosa. The main muscular coat is moderately infiltrated with wandering leucocytes, but is otherwise normal, as is the peritoneum.

Lymphatic Gland.—Here the principal lesion is the presence in the lymph sinuses of large cells of an endothelial type, which are probably the result of proliferation of the reticulum cells. The general architecture of the gland, with distinction between follicular substance and sinuses is preserved. This condition is the so-called irritative hyperplasia of lymphatic nodes, and is not of especial significance.

Diagnosis.—Lymphangiectasia cavernosa of the intestinal submucosa, with inflammation and hyperplasia of the same coat. Irritative hyperplasia of the mesenteric lymphatic nodes.

The wide extent of the dilatation of the submucous lymphatic vessels is most remarkable. No positive evidence of the formation of new lymphatic vessels is apparent, so that the case is interpreted as dilatation of the pre-existent lymphatics of the submucous coat of the intestine. The cause of the lymphangiectasis is not apparent in the sections. Nor can a definite statement be made concerning the contents of most of the larger cyst-like spaces. In the sections these are empty. As already stated, some coagulated lymph and fibrillated fibrin can be seen in some of the spaces, and in others, especially the smaller ones, there are many leucocytes; but, unfortunately, the sections do not show the contents of the larger spaces.

Discussion.

Dr. W. G. MacCallum had seen the sections in Baltimore, at the time that Dr. Welch examined them. The point of greatest interest was the nature of the contents of these cavities and of the walls of the cavities themselves. He had not been able to convince himself that all the cavities represented lymph channels. It would be interesting to know what bacteria were found.

Dr. Blatteis said that no definite organism was present in any of these spaces.

Dr. MacCallum thought that the inflammatory reaction suggested the possibility that there were organisms present. He would like to know whether there had been any gas present in the cavities, which could not be determined by mere microscopic inspection. He had tried unsuccessfully to elicit crepitation in the specimen presented. He had also seen the case to which Dr. Whipple had referred, that of a student who had lived for some years in Turkey; but he saw no points of resemblance in the two cases. In Dr. Whipple's case there was a very remarkable deposit of fat and fatty acids in various places in the mesenteric glands and elsewhere.. The suggestion was made by Dr. Whipple largely on account of the presence of fat, and it seemed possible that fatty acids might have been extracted in this case.

Dr. Eli Moschcowitz said that within the past day or two he had dissected a case in which a similar picture was found in the wall of the stomach. As yet no sections had been made, but macroscopically the lesion appeared identical with that presented by Dr. Blatteis. The specimen occurred in a patient who had carcinoma of the head of the pancreas. The gastro-hepatic omentum was densely infiltrated with carcinoma and the glands along the lesser curvature were the seat of large metastases. Especially significant was the fact that the honey-combing of the submucosa was particularly prominent in the neighborhood of the lesser curvature, becoming less and less marked toward the greater curvature. He thought that the condition was probably a lymphangiectasis due to obstruction of distal lymphatics, and he suggested that in Dr. Blatteis' case there was a lymphatic obstruction in the mesentery, corresponding to the drainage area of the affected part of the colon, which in all probability would eventually reveal itself.

DR. O. H. SCHULTZE was reminded of a case of phlegmonous gastritis which he had seen several years ago. The description was not definite as to whether this case was really a lymphangiectasis. Were these cavities definitely lined with epithelial cells? The question of the bacteria present was important.

DR. JAMES EWING suggested that the investigation of this case should include the mesentery and other portions of the intestinal wall. He had examined the sections with care and interest. The description given was clear, except that in the sections which he had looked at the spaces were usually lined by giant cells of the foreign body type, such as appear in inflamed fat tissue. He thought he had detected traces of fecal matter in some spaces. He would suggest that the condition had resulted from inflammation and degeneration of the submucous fat tissue.

DR. BLATTEIS said that there was no crepitation in the fresh specimen. The spaces were apparently empty, at least they were macroscopically empty. No definite contents could be determined—cystic, fecal, or otherwise. There was apparently no obstruction anywhere higher up. The clinical history was against the suggestion of a phlegmonous inflammation; the temperature of the patient never exceeded 100.6°, and the patient recovered.

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DR. RICHARD M. PEARCE, *President.*

A NEW METHOD FOR THE ESTIMATION OF CRANIAL CAPACITY AT AUTOPSY.

BY A. J. ROSANOFF, M.D., AND JOHN I. WISEMAN, M.D.

It has been shown by the researches of Bartels,[1] Pfleger,[2] Bolton,[3] Mittenzweig,[4] Southard,[5] Watson,[6] and many others that the average weight of brains of insane subjects is below the normal average; and it has also been shown that when cases of idiocy and imbecility, epilepsy, general paresis, and coarse cerebral lesions are excluded from consideration, the average is still found to be below the normal.

The questions that at once suggest themselves are: How often and in what clinical types of cases is this reduction in weight due to a process of atrophy? How often does it constitute an original defect?

In this paper we purpose to discuss: (1) the methods that are generally employed for the detection of atrophy; (2) existing methods for the estimation of cranial capacity; and (3) a new method proposed by us.

1. *Methods Generally Employed for the Detection of Atrophy.*

Within the past four years one of us has had occasion to examine a very large number of post-mortem records in five large hospitals for the insane in this State and in five large general hospitals in New York and in Boston. The only points that were found to be recorded as having a bearing upon the question of brain atrophy were brain weight; certain gross appearances, such as shrinkage of gyri, widening of sulci, and excess of cerebrospinal fluid; and certain microscopical appearances. A review of the literature pertaining to this subject has also shown that with some few exceptions—notably the recent work of Reichardt[7]—no attempt has been made to apply more accurate methods even in special investigations.

The fact that brain weight varies normally within wide limits renders the record of such weight alone in a given case of but little value. For it is obvious that a brain may be found at autopsy to be as high as the normal average in weight, or even higher, and yet may be one in which atrophy to the extent of 200 grams has occurred. And it is equally obvious that a brain may weigh 200 grams less than the normal average and yet may be one in which no atrophy has occurred.

Estimation of degree of atrophy from gross appearances, such as shrinkage of gyri and widening of sulci, is at best but roughly approximate, there being no way of taking exact measurements. Indeed, when the atrophy is but slight or moderate, as it is in most cases, its very existence may escape detection if judgment is based on these gross appearances.

Increase of cerebrospinal fluid as a measure of atrophy also has sources of large error. In the first place it is difficult to drain and collect all the fluid from the subdural and subarachnoid spaces and from the ventricles; in the second place it is difficult to prevent an admixture of blood and serum from the severed blood vessels; in the third place there is no way of judging what proportion of the fluid is derived from the cranial cavity and what proportion from the spinal canal; and in the fourth place encroachments upon the cranial cavity resulting from thickening of the dura, formation of false membranes due to pachymeningitis, etc., would fail to be taken into account.

It would seem safe to say, without going into an extended discussion, that microscopical methods are still less helpful than the methods already discussed in estimating degree of atrophy.

In the meantime, parallel with the anatomical observations showing that the average weight of brains of insane subjects is below the normal average, there are gradually accumulating clinical observations showing, on the one hand, that insanity is most apt to develop in persons of inferior or at least vulnerable mental make-up, and on the other hand, that most forms of insanity gradually lead to functional deterioration.[8]

These considerations have directed our interest to the development of a convenient method by means of which atrophy, even when present in but slight degree, can be detected, so that cases of low brain weight resulting from atrophy may be distinguished from those due to original defect.

Assuming that there is some correspondence between cranial capacity and brain weight, and that the ratio representing this correspondence can vary normally only within narrow limits, we sought to develop a practical method for the estimation of cranial capacity, since cranial capacity seems to be the only available criterion of judgment as to the original weight of the brain in any given case.

Our plan is to find by means of a large number of measurements the normal ratio between cranial capacity and brain weight. Any increase of this ratio in a given case would indicate abnormal reduction of the brain mass, which, in the absence of evidences of compression, would be attributable to atrophy.

2. *Existing Methods for the Estimation of Cranial Capacity.*

The methods that have been proposed for the estimation of cranial capacity depend upon the employment as filling material either of metallic shot, glass beads, or peas, or of liquids, principally metallic mercury and water.

As between shot, beads, and peas, beads are preferred, shot being heavy and peas having the disadvantage of swelling from contact with moisture and shrinking again on being dried, therefore giving inconstant results.

Glass beads are quite suitable and under certain conditions capable of furnishing reliable results. Thus in a series of one hundred estimations made in Prof. von Török's[9] laboratory by Kelemen the maximum error was a trifle over 1.5 per cent. In this series of estimations a bronze model of a skull, the same selected lot of beads, and the same measuring cylinder were used throughout. These conditions, however, are not like those under which at most autopsies estimations of cranial capacity must be made. It would seem that if this method were generally adopted the extent and frequency of error would inevitably be much greater than in the case of Kelemen working under artificial and strictly uniform conditions. The slightest irregularity in the shape of the beads, a lack of uniformity in their size, failure to use a measuring cylinder of exactly the same shape and size in every estimation would very materially affect the accuracy of the method.

As regards methods which depend upon the use of liquids as filling material, we fully agree with von Török who considers them all, with possibly one exception which we shall refer to later, as entirely untrustworthy. Yet quite recently Reichardt has again suggested such a method. He insists upon a very straight saw cut, upon estimating the cranial capacity before sectioning the thorax and abdomen, and upon repeating the estimation in each case at least ten times, disregarding the results obtained in the first three or four estimations, and using only the calculated average of the results of the last six or seven estimations.

Reichardt himself points out some of the sources of error. Thus he states: "Our investigations have taught us that even slight irregularities of the saw cut may cause an error to the extent of minus 300 c. c." He states also that leakage into the foramen magnum, the smaller basal foramina, and the large blood vessels may cause great error, to obviate which he recommends pouring water into the base of the skull until the level at these points of leakage remains constant for several minutes. In some cases, he states, it may be necessary to use corks, putty, or non-absorbent cotton for sealing up the points of leakage.

There are still other sources of error which Reichardt does not mention. Failure to insure a perfectly horizontal position of the level of the saw cut in filling either the base or the calvarium would necessarily involve great error, for it must be remembered that the circumference of the skull is so wide that a difference of 1 mm. in depth of the water makes a difference of about 30 c.c. in the reading.

It must be noted, however, that Reichardt does not claim for his method absolute accuracy. He maintains merely that with the exercise of some care the error involved in the use of his method may be reduced to within 50 c.c., and he maintains further that an error of such degree would not affect the practical usefulness of his method. The latter assumption we believe to be untenable, for all available data show that importance attaches precisely to the slighter reductions in the brain weight, so far as the functional insanities are concerned, the coarser reductions being observed mainly in connection with arrests of development and with organic brain lesions.

We have still to consider another method which has been devised by Poll.[10] The essential feature of this method consists in the use of a bag, made of very thin rubber, which is placed in the cranial cavity and through a trephine opening filled with water. The rubber is so extensible that it is supposed that the mere weight of the water is sufficient to cause the bag to bulge so as to fill every irregularity in the cranial cavity. Poll and later von Luschan have obtained by the use of this method results with error of less than 1 per cent. By an ingenius experiment von Török has shown that it is very difficult, if at all possible, to make the bag actually fill every irregularity in the cranial cavity. He covered the inside of a dry skull with sticky colored crayon; then in testing Poll's method he found that the rubber bag failed in many spots to get an impression of the crayon, showing that at those spots it did not come in contact with the skull bones.

Aside from the possible inaccuracy of Poll's method, its inconvenience and the difficulty of obtaining the necessary rubber apparatus—which does not appear to be on the market—would render that method unsuitable for common use, and therefore not likely to be generally adopted.

It seemed to us, therefore, that there was still a need for a simple yet sufficiently accurate method for estimating cranial capacity.

3. *Description of the New Method.*

The special feature of our method consists in the use of putty as filling material. The details of technique are as follows.

No special care needs to be exercised in opening the skull; it is necessary to guard only against extensive cracking or chipping out of large fragments of bone. The angular or so-called undertaker's saw cut is to be preferred to the circular one. The dura is incised and the brain removed in the usual manner. The dura is then carefully stripped from the base of the skull and cut away by a circular incision made as far below the foramen magnum as possible. The foramen magnum is now closed by means of a cork stopper of suitable size pressed down until its upper edge no longer protrudes above the internal surface of the occipital bone but is on the same level with it. The base of the skull is then filled with putty, small lumps being used at first which are carefully pressed in so as to fill all the irregularities. The calvarium is filled with putty in a similar manner, after which it is replaced and by pressure part of the excess of putty is squeezed out through the saw cut. The next step is to fit the calvarium over the base of the skull as exactly as possible and here slight irregularities and angles in the saw cut are very helpful. The final fitting is most readily accomplished by gentle tapping with a wooden or rawhide mallet upon the top of the skull and carefully removing the excess of putty as it appears through the saw cut.

The putty as used for this purpose must be much softer in consistency than as used ordinarily by glaziers. It may readily be softened by being kneaded with linseed oil, and if too soft it may be made firmer again by the addition of whiting.

The putty is best kept under water; this prevents it from drying and renders it unnecessary to soften it afresh every time that it has to be used.

It is advisable to keep the hands wet with water to prevent the putty from sticking to them. Generally the moisture which covers the inside of the skull prevents the putty from sticking to the skull bones. Sometimes it does stick slightly in places, but it can always be easily and completely removed.

We use for measurement two glass cylinders of 2,000 c.c. and 1,000 c.c. capacity respectively. The smaller cylinder is filled with water exactly up to the 1,000 c.c. mark. About 200 c.c. is then poured over into the larger cylinder. The putty from the cranial cavity is then put into the large cylinder preferably in small lumps rolled up and allowed to slide down slowly by inclining the cylinder to prevent splashing of the water. After all the putty has been put into the cylinder and gently pressed down with a stick, more water is poured in from the smaller cylinder until the level is exactly at the 2,000 c.c. mark, care being taken that no bubbles of air are caught underneath or between the lumps of putty. The reading is now taken on the smaller cylinder. By deducting from 2,000 the number of cubic centimeters which were taken from the smaller cylinder to fill the larger one, the figure representing the cranial capacity in cubic centimeters is obtained.

4. *Results Obtained in Twenty Autopsies.*

We present the results obtained in a small number of autopsies merely to show that the method is trustworthy and that it reveals evidence of atrophy in cases in which brain weight alone fails to show it.

Our results have been tabulated so as to show in each case the race, sex, age, height, and weight of the subject; the clinical classification; the weight of the brain and that of the dura; the cranial capacity estimated one, two, or three times; and the calculated ratio between cranial capacity and brain weight.

The close correspondence between the results obtained by repeated estimations in the same cases show that the method is trustworthy. In all cases but two, variation of the results was within the limits of less than 1 per cent. In the two cases in which the variation was higher (though still within the limit of less than 50 c.c. regarded by Reichardt as permissible) the discrepancy was ascribed to the fact that in opening the skull the calvarium was badly cracked.

The ratio between cranial capacity and brain weight is shown in our table to be very variable in pathological cases. Its full significance will, however, become apparent only when a large number of observations upon normal as well as insane subjects have been made.

[1] *Neurol. Centralbl.*, 1887, p. 261.
[2] *Jahrb. f. Psychiat.*, Vol. 3, p. 107.
[3] *Jour. Ment. Sci.*, Apr., 1905, p. 20.
[4] *Allg. Ztschr. f. Psychiat.*, 1905, p. 31.
[5] *Am. Jour. of Insan.*, Apr., 1910, p. 673, and July, 1910, p. 119.
[6] *Jour. Ment. Sci.*, Apr., 1910, p. 227.

[7] Ueber die Untersuchung des gesunden und kranken Gehirnes mittels der Wage. Jena, 1906.

[8] Adolf Meyer: An Attempt at Analysis of the Neurotic Constitution. *Am. Jour. of Psychol.*, 1903, p. 90. August Hoch: A Study of the Mental Make-up in the Functional Psychoses. *Jour. Nerv. and Ment. Dis.*, Apr., 1909, p. 230.

[9] Von Török: Ueber ein neueres Verfahren bei Schädel-capacitäts-Messungen, etc. *Virchow's Arch. f. path. Anat.*, 1900, p. 248.

[10] Described by von Török, *loc. cit.*

TABLE SHOWING RESULTS OF TWENTY AUTOPSIES

No.	Name	Color	Sex	Age	Height	Weight	Diagnosis	Weight of Brain	Weight of Dura	Cranial Capacity			Cran. Cap. Brain Wt.
										1st Estimati'n	2nd Estimati'n	3rd Estimati'n	
273	A. P.	White	M	48	163 cm	55.79 kgm	Manic-depr. ins.	1517 gm.	84 gm.	1650 c.c.	1643 c c.	....	1.0857
275	H. D.	Negro	F.	29	149 cm.	....	" " "	1317 gm.	43 gm.	1422 c c.	1460 c.c.	....	1.0941
277	J.H.B.	White	M	57	171 cm.	52.84 kgm	" " "	1440 gm.	49 gm.	1620 c.c.	1605 c.c.	....	1.1201
281	J. G.	"	M.	50	171 cm.	58.97 kgm	" " "	1500 gm.	69 gm.	1683 c.c.	1690 c.c.	....	1.1247
263	H. G.	Negro	F.	22	148 cm	78.93 kgm	Dementia præcox	1015 gm.	....	1225 c.c.	....	....	1.2069
274	K. N.	White	F.	68	161 cm.	86.18 kgm	" "	1192 gm.	81 gm.	1340 c.c.	1348 c,c.	1342 c.c.	1.1275
280	L. F.	"	F.	61	155 cm.	....	" "	1265 gm.	67 gm.	1440 c.c.	1437 c.c.	....	1.1375
278	T. B.	"	M.	62	172 cm.	63.96 kgm	Polyneuritic psychosis	1439 gm.	67 gm.	1673 c.c	1667 c.c.	....	1.1605
267	M.L.U.	"	F.	65	146 cm.	40.37 kgm	Epilepsy	1134 gm.	35 gm.	1200 c.c	....	....	1.0582
272	E. D.	Negro	M.	51	160 cm.	....	Imbecility	1141 gm.	55 gm.	1355 c.c.	1360 c.c.	1350 c.c.	1.1876
279	B. M.	White	F.	90	136 cm	....	Senile dementia	1010 gm.	40 gm.	1360 c c	1357 c.c.	....	1.3455
283	J. C.	"	M.	71	170 cm.	72.58 kgm	" "	1368 gm.	65 gm.	1590 c.c.	1583 c.c.	....	1.1579
265	J M.	"	M.	33	160 cm.	45.36 kgm	General paresis	1352 gm.	57 gm.	1555 c.c.	....	....	1.1501
266	S. L	"	F.	39	149 cm.	....	" "	984 gm.	39 gm.	1355 c,c.	....	....	1.3770
268	H. S.	"	M.	59	157 cm.	50.35 kgm	" "	1204 gm.	79 gm.	1515 c c.	....	....	1.2583
269	B. M.	"	M.	75	161 cm	65.32 kgm	" "	1352 gm.	77 gm.	1565 c c.	1577 c.c.	....	1.1619
271	J. R.	"	F.	55	161 cm.	....	" "	....	70 gm.	1643 c.c.	1657 c.c.	1645 c c.	....
284	J. L.	"	M.	56	180 cm.	72.58 kgm	" "	1335 gm.	60 gm.	1545 c.c.	1540 c.c	....	1.1558
282	E. F.	"	F.	75	140 cm.	....	Cerebral softening	1140 gm.	69 gm.	1397 c.c.	1397 c,c.	....	1.2254
270	J. M.	"	M.	80	155 cm.	79.38 kgm	Unclassified	1307 gm.	....	1527 c.c.	1485 c.c.	....	1.1530

Discussion:

Dr. W. G. MacCallum was of the opinion that Dr. Rosanoff's method deserved credit for its simplicity and accuracy. He said that he should like to ask Dr. Rosanoff whether he had arrived at a definite idea of how much space is occupied by the dura and blood vessels, and whether the fluid which is accumulated in ordinary cases varied very much under ordinary circumstances, and whether it has to be taken into consideration in this method. Of course, he understood that the method gave the absolute cranial capacity after the dura had been removed.

Dr. Rosanoff replied that his method gave the absolute cranial capacity after the dura had been removed. All of his cases were cases of insanity, but not in all was there any evidence of atrophy. In cases in which there was no evidence of atrophy, the difference between the figures representing the cranial capacity and the figures representing the brain weight, was less than 100. In some cases in which there was very marked atrophy, the figure was above 200, and even much more than that. In one case the brain weight was 1,500 g., and the cranial capacity 1,690 c.c., a difference of 190. This was a case of a white male, suffering from manic-depressive insanity. Another case was one of senile dementia, in which the brain weight was 1,010 g., and the cranial capacity 1,360 c.c. The dura in the first case weighed 69 g., and in the second, only 40 g.

Dr. J. H. Larkin asked Dr. Rosanoff whether he had made any comparisons between putty and plaster-of-paris. He stated that some investigators had had very great success with plaster-of-paris impressions. There seemed also to be some difficulty in the pliability of putty in securing an impression of the cranial cavity, as putty was very variable and offered great difficulty in its application. The conclusion, he thought, seemed to be that plaster-of-paris which had been through a certain process whereby hardening did not readily take place, gave impressions which were more thorough and scientific. The application of the method advanced by Dr. Rosanoff, while not exactly new to him, offered some mechanical difficulties. Dr. Larkin's question, however, was merely on a point of information, as he had taken several measurements himself, but had given some of them up on account of the unreliability of putty, and now relied entirely upon the plaster-of-paris method.

Dr. Rosanoff, in reply to Dr. Larkin, said that for taking an impression of the cavity, plaster-of-paris would probably be very satisfactory. But his method was for the purpose of volumetric measurement only. Dr. Rosanoff said that plaster-of-paris, after becoming solid, and after immersion in water to ascertain the volume, would absorb enough water to render the method liable to considerable error. Moreover, the composition of putty was of no moment, as it was quite suitable for determining the volume of the cavity. The error that does creep in is within 1 per cent., this last being due apparently to the difficulty of fitting the skull cap over the base of the skull with sufficient accuracy.

STUDIES IN HEREDITY IN CANCER OF THE WHITE RAT.

I. LEVIN, M.D., AND M. J. SITTENFIELD, M.D.

It is hardly possible to come to a definite conclusion at present in regard to the influence which heredity exerts on the occurrence of human cancer. A study based on a statistical analysis of hospital cases seems to indicate that this influence is very small. But the material is most probably not well suited to this inquiry. More promising results ought to be expected from an analysis of the so-called "cancer families" in accordance with the modern methods of genetics. This method consists in collecting data not only of the members of the family suffering from cancer, but also of all the other normal members of the same family. All the members are then divided into respective generations of relationship to each other and then the numerical difference is studied between the cancer cases in the different generations of a "cancer family" and an apparently normal family used as a control. This method will most probably enable us to approach the solution of the question in human cancer. But the work is just barely begun and it will require a great deal of study before conclusions can be drawn.

It would seem *a priori* that it is a great deal easier to study the subject experimentally on cancer of the white rats or mice. The life cycle of these animals is only about two years and during the decade of extensive research on the tumors of these animals there were many opportunities to obtain several generations of the same stock. But thus far there has been little accomplished in the matter.

Bashford approached the subject experimentally in the following way: He removed surgically tumors occurring spontaneously in white mice, bred these mice with each other or with the offspring of cancerous parents, and then studied the frequency of the occurrence of cancer in the offspring. The work has continued for several years, and it has not been possible to detect any evidence that the liability to cancer has been enhanced by systematic in-breeding. The difficulties in an analysis of the results of this method of research are apparent and similar to the difficulties that obtain in an analysis of simple statistical data in regard to heredity—namely, the whole number of cases in the offspring is so small that no correct comparison can be made with the percentage of tumors occurring in stock animals of the cancer age.

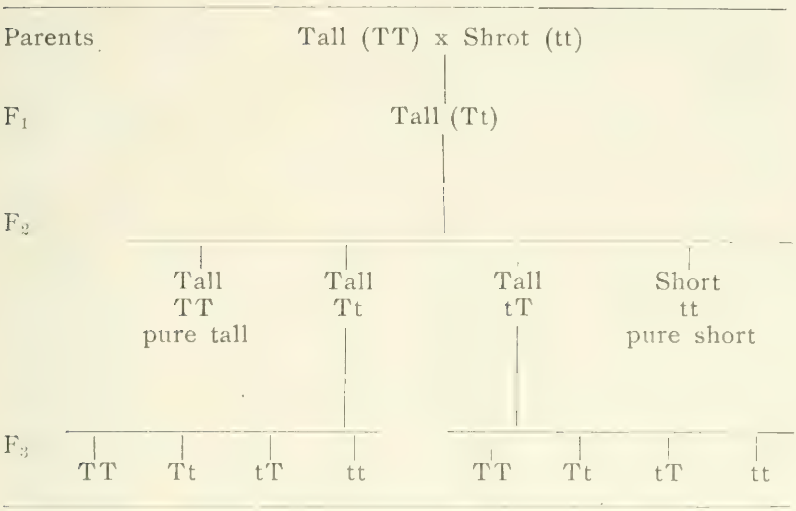
Tyzzer attacked the subject from a different standpoint. He studied the influence of heredity in mice with reference to their susceptibility to transplantable tumors. He found that a certain tumor which originated in a Japanese waltzing mouse was very readily transplantable in this variety of mice, but could not be transplanted at all in a common albino mouse. He then crossed the common albinos with Japanese waltzing mice and inoculated the Japanese tumor into the offspring. His results showed that the hybrids of the first generation were then slightly more susceptible to the tumor than the Japanese waltzing mice, but the hybrids of the next generations, second as well as third, proved to be absolutely insusceptible to this tumor. Tyzzer concludes that the susceptibility of an animal to an inoculable tumor is neither inherited in accordance with Mendel's law, nor are the results obtained from cross breeding explained by any other known principle of inheritance.

While the study of inheritance in transplantable tumors of the mouse or rat offers less possibility for direct analogies with heredity in human cancer than studies on spontaneous cancer of the same animals, the ease with which experiments can be varied in transplantable tumors offers better promise for solving the question, and it seems to be clear from Tyzzer's results that there exists a certain kind of hereditary transmission in these tumors. But Tyzzer's method is too complex for a clear analysis in accordance with modern studies on genetics.

It may be well to present here in a few words the salient features of the science of genetics, as studies on heredity are called at present. The fundamental laws of the science were discovered by Gregor Mendel in 1865, but they passed unnoticed until they were re-discovered simultaneously by de Vries, Correns, and Tschermack in 1900. Mendel subjected to an experimental analysis the commonly known fact that an offspring may resemble in its different traits of character one or the other parent. He argued that a multicellular organism develops not from a single germ-cell or gamete, as it is called in genetics, but from a zygote, by which is meant the resultant of the union between the paternal and maternal gametes. Consequently, in order to learn the fate of parental characteristics in the offspring, certain simple features have to be selected in each parent and studied in the following generations. These simple features are called unit-characters, and in order to be able better to see the results of breeding, Mendel selected for his studies pairs of opposite unit-characters. For instance, in his studies on inheritance in edible peas (*Pisum sativum*) he selected for one parent a tall specimen and for the other a dwarf one. The cross-breed of such a union is not a specimen of middle height, but all the offspring have the height of the tall parent. This fact of segregation of unit-characters represents the fundamental law in Mendelian inheritance. By this is meant the phenomenon, that when of two parents one possesses a certain unit-character, this appears in one offspring and is absent in the other. The former condition is called dominant and the latter recessive.

Thus of the offspring of two parents with opposite characters, the first hybrid generation (F1), according to Mendelian writings, all present apparently only the dominant character. When this offspring is in-bred, there shows itself in the next generation of hybrids (F2) a complete segregation of character; not all the offspring possess the same dominant unit-character, but only 75 per cent. show the dominant character and 25 per cent. the recessive.

Now, if the entire F2 offspring should be divided into four parts, of which three show the dominant character and one the recessive, and then the different members should be inbred, the results will show that the recessive quarter will always give only a recessive offspring, or, as it is called in modern nomenclature, will *breed true* to its character. One-third of the dominant offspring will also breed true to its dominance, while the remaining two-thirds of the dominant, or consequently one half of the entire F2 offspring, on in-breeding, will be *cross-bred* and will result again in three-fourths dominant and one-fourth recessive. These results indicate that a hybrid animal showing the recessive unit-character will always breed true, while in the dominant hybrids some are true dominants and others contain both units. The following table of Dr. Bateson's clearly illustrates this scheme of Mendel's theory:



These so-called Mendelian laws of inheritance are easily demonstrated when one deals with simple characteristics like height, or color of flowers, etc.; but it must be understood that it is frequently extremely difficult to show clearly these Mendelian laws in breeding experiments, in view of the fact that each parent, and consequently so much more, the hybrid, possesses a great variety of unit-characters. It is furthermore shown that while certain characters segregate, in the Mendelian meaning of the term, others again blend and appear as a new character in the offspring. Even when one deals with a species which contains only a combination of segregating characters, the interaction between the latter may obscure results. The difficulties increase greatly when the investigation does not deal with simple unit-characters, but with the extremely complicated condition of the susceptibility of an animal to tumor growth.

It is well known that racial differences play an important role in the susceptibility of mice and rats to inoculable tumors, and it is natural to suppose that the hybrids of the waltzing mouse and common albino contain several unit characteristics exerting their influence on the susceptibility to the inoculated tumor. This is probably the reason why there was apparently no regularity in Tyzzer's results. It is very interesting to note in this connection that he obtained different results in two sets of hybrids of the same first generation where the difference consisted in the fact that the common albino parents came from different stocks.

The first requirement for successful experimentation in genetics consists in selecting objects that will have as few opposite characteristics as possible. It seemed to the writers as the best plan of work to select as the only unit-characters to work with, the susceptibility or resistance of an animal to an inoculated tumor, but otherwise to in-breed within the same race. The work may be pursued in one of the following two ways: Either select tumor-bearing animals, remove surgically the tumors, and cross them; or else select animals that appear to be resistant to the inoculation. While both methods will be employed before final results are reached, it was to be expected that the offspring of immune animals would offer more striking results, since normally only a small percentage of the animals is resistant. Therefore the latter method was selected for the beginning of the work.

The results of the investigation obtained thus far, while not final, are so suggestive that it was considered advisable to offer them here. The experiments were done with Ehrlich's sarcoma of a white rat, a tumor of a very malignant type, which takes in from 80 per cent. to 100 per cent. of the animals.

Tumor resistant rats, or "Nullers," as Ehrlich calls them, were in-bred. Four litters were obtained of which the offspring lived long enough to be inoculated with the tumor. One litter of eight rats was born on the 15th of May, the second litter of six rats on the 19th of May, the third litter of seven rats on the 24th of May, and the fourth litter of two rats on the 2nd of June. On the 12th of August all the hybrid rats and twenty normal control rats, whose age and size were known and corresponded closely with the offspring of the Nullers, were inoculated with the tumor. The following table presents the result of the inoculation:

	Offspring of Nullers.	*Controls.*
No. of rats inoculated with tumor	23	20
No. of rats surviving at final examination	20	14
No. of rats with tumors	5	12
Per cent. of takes	25	86

The analysis of the table shows that while the tumor took in 86 per cent. of the control rats, it took in only 25 per cent. of the offspring of the Nullers. The result is very striking and tallies closely with Mendelian expectations.

The usual stock of white rats contains both resistant and non-resistant individuals, consequently a pair consisting of a resistant male and a resistant female would present, in Mendelian terminology, a first filial generation (F1) and the twenty rats bred from this first generation would represent the second generation (F2). Of these twenty rats fifteen were resistant and five non-resistant, showing a ratio of 3:1. Consequently, resistance to the growth of cancer in the white rat behaves like a dominant unit-character.

It is true that it is extremely difficult to interpret in accordance with the rules of genetics pathological conditions like a tumor growth, where the real pathogenesis is not yet clear. The objection may be urged, for instance, that the resistance was not transferred in this case through the gametes, but that certain antibodies circulating in the blood of the mother may have been transferred to the offspring through the placental circulation. In view of this, another set of experiments will be undertaken, where only the males are resistant. But even now it would seem to be difficult to explain on the assumption of placental transfer, that not all of the offspring became resistant, when both parents presented that characteristic, but only a certain percentage of the offspring, and that the percentage so closely coincides with the Mendelian expectations. Besides, this is not the only instance in which resistance to a disease seems to depend on the presence in the germ cell of a Mendelian unit. There exist certain kinds of wheat which are very susceptible to a disease known as wheatrust, which is due to an infection with a fungus. Other varieties of wheat are immune to the disease. Biffen demonstrated that when an immune strain is crossed with a susceptible one, the first filial generation consists of susceptible strains only, while in the next generation there appear susceptible and immune strains in the ratio of 3:1—showing that in this case the susceptibility is the dominant unit-character.

As was stated above, the work has just begun. Experiments are under way with tumor-bearing animals, with crosses between resistant and non-resistant, and also with in-breeding in the following generations. But the results obtained thus far seem to be extremely suggestive and it appears possible that work of such character may be of importance both in the further elucidation of the questions in heredity and in the pathogenesis of cancer.

THE CONDUCTING SYSTEM OF THE HEART: ITS NORMAL ANATOMY IN MAN AND CERTAIN OTHER MAMMALS.

A. E. COHN, M.D.

Dr. A. E. Cohn demonstrated lantern slides showing the path of the conduction system of a horse's, a cow's, a dog's, and a human heart. The histology of the nodes was likewise demonstrated.

1. Section through the right auricle of a dog's heart, showing the sinoauricular node.

2. Sinoauricular node, from a child's heart.

3. Section of the membranous septum, showing the auriculoventricular node. The structure of this node is practically identical with the structure of the sinoauricular node.

4. Section of a cat's heart, showing rather more plainly the way in which the bundle divides.

5. Section of a rat's heart, taken from above downward, showing the relation of the conducting system to the interventricular septum.

6. Section of the same human heart shown before, taken from just where the membranous septum ends.

Sections were also shown of the glycogen content in a sheep's conduction fibers (Nagayo) and of Purkinje cells from a beef heart.

Discussion:

Dr. H. A. Stewart remarked that it was gratifying that Dr. Cohn had paid some attention to the nervous components of the bundle of His. The tendency, he said, in working on the anatomy of the bundle of His had been to disregard such a thing as a nerve; even Tawara himself made only a very cursory mention of the fibres in the auriculoventricular bundle. He added that those who have supported the old neurogenetic theory could now hold up their heads with some confidence. As Dr. Cohn had already mentioned, Dr. Wilson of Chicago had produced a luminous article on the nerves of the auriculoventricular bundle. Dr. Stewart had had the pleasure of seeing sections made by Dr. Wilson, who had been able to demonstrate very clearly the presence of ganglion cells in the auriculoventricular bundle, the fibers being of a very distinctive character, running in bundles between the muscle fibers and cells. So that here there was a clear demonstration, not only of the fibers, but also of ganglion cells of a very complex mechanism. Those who have upheld the myogenetic theory have said that it is the muscular part of the bundle which conducts impulses, because this muscular part is found very early in the embryo; that it remains unchanged throughout life, and is unaffected by atrophy or hypertrophy. But there is no known physiological experiment which has proved that the conduction between the auricle and the ventricle is by muscle. Dr. Cohn had already very forcibly pointed this out. The working out of the details of the nervous mechanism will finally establish, without doubt, the correctness of the view that the conduction is by nerves, instead of by muscle.

A CASE OF PULMONARY STENOSIS.

CHARLES NORRIS, M.D.

Dr. Charles Norris presented a case of pulmonary stenosis in a child of six years, which up to within four weeks of death, had been in apparently perfect health. There was no history of syphilis or other previous illness except measles. A month before its admission to Bellevue Hospital the child's mother observed that its face was swollen, and from then on it ceased to play. It was taken to the hospital, where it rapidly developed general subcutaneous edema and ascites, but no pleural effusion. There was marked cyanosis.

At the autopsy there was found a tremendous hydropericardium, the pericardial sac occupying the whole anterior portion of the chest. The heart as a whole was about normal in size, but there was an extreme hypertrophy of the right heart. The right auricle was markedly hypertrophied with closed foramen ovale. There was a slight tricuspid stenosis with fresh, very minute verrucae. The pulmonary cusps showed an extreme stenosis barely admitting a small probe. The valves were large and greatly thickened and there was an extreme hypertrophy of the right ventricle, so much so that the normal relation as to size between the ventricles was reversed. The septum bulged into the left ventricle but was in no place defective. There was a slight nodular sclerosis of the mitral valve. The ductus arteriosus was closed.

CALCIFICATION OF THE HEART MUSCLE FIBERS.

ALWIN M. PAPPENHEIMER, M.D.

A most unusual site for the abnormal deposition of calcium salts is the striated muscle of the heart. Rokitansky in the third edition of his text-book (1856) describes an instance of this lesion in the following words: "the muscle-fibers were transformed into rigid, brittle, refractile rods." Von Recklinghausen refers to the condition, as does Orth in his Lehrbuch; neither writer gives a detailed description. The modern text-books either ignore the lesion, or content themselves with the mere mention of its possible occurrence. Hart,[1] in a recent article, was able to collect but thirteen cases from the literature.

Besides the case here reported, we have seen sections from a case of Dr. Heinecke in Leipzig which showed an identical lesion; but in the routine examination of many hundreds of sections of heart muscle, we do not recall a similar finding.

The patient in our case was a male, twenty-one years of age. He was admitted to the service of Dr. Rogers at Bellevue Hospital in November, 1909, and operated upon for acute gangrenous appendicitis with peritonitis. Following the operation and continued drainage there was a general subsidence of all acute symptoms. On December 14th, however, the patient developed a fecal fistula; on the following day his temperature rose, and from this time until his death, eight months later, he showed symptoms of chronic sepsis, with chills, high remittent fever, continued leucocytosis, progressive anemia and emaciation. Three operations for supposed subphrenic abscess failed to disclose the true condition. The medical treatment consisted in the administration of colon vaccines and thyroid globulins.

At the necropsy, there was found suppurative pylephlebitis, with recent thrombosis of the portal vein; multiple large abscesses of the liver; abscesses of the right lung; a large hypernephroma of the right adrenal, which showed a diffuse suppurative infiltration; a recent fibrinous pericarditis; marked degeneration of the kidneys, and a fecal fistula at the site of the old operation, walled off by adhesions.

The heart muscle is described in the protocol as being "extremely pale, soft, yellowish-brown."

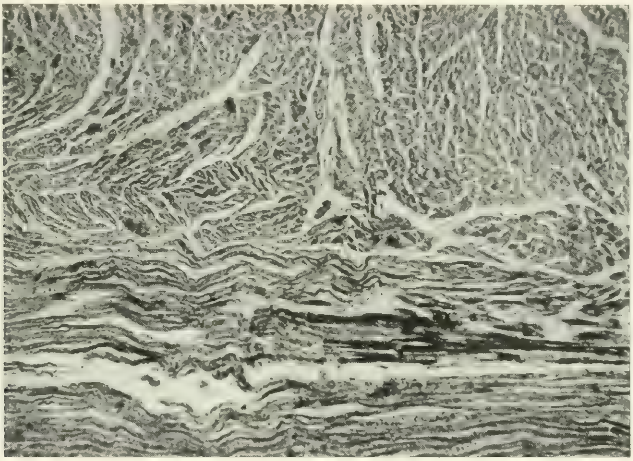
The lime deposits in the myocardium of the left ventricle were discovered in the course of the routine histological examination. We can say nothing, therefore, as to the distribution of the calcareous areas, only a small piece being available for study. In all the sections examined, there were found sharply circumscribed groups of fibers impregnated with lime salts—as many as a dozen foci in a section roughly 1.5 by 0.5 cm. in size. The staining reactions are typical of lime salts; an intense blue with Delafield's hematoxylin, black with Heidenhain's iron hematoxylin, and with 5 per cent silver nitrate after the method of von Kossa. Upon the addition of the acetic acid to an unstained section, there is no evolution of gas noted; carbonates, if present, cannot be demonstrated.

The calcification is sharply limited to the muscle fibers themselves, and even with the delicate silver nitrate method, no granules can be found in the interstitium. Either the deposit is in the form of coarse granules, which occasionally are arranged in transverse and longitudinal rows following the discs and primitive fibrils; or the entire fibre, together with its lateral anastomoses, is diffusely impregnated. The contours of the calcified fibers are somewhat irregular, and the calcareous fibers appear somewhat thicker than the normal fibers in the vicinity. On the cross section, one sees that the entire fiber is not always uniformly affected. The lime may be deposited first either in the center or near the surface or in the form of scattered granules. In fibers cut longitudinally, only a segment of the fiber may be impregnated, or the process may be complete in one portion and but slightly indicated in another.

A careful study with Mallory's phosphotungstic and Heidenhain's iron hematoxylin stains has convinced us that the deposits of lime take place only in fibers which are the seat of advanced degenerative changes or complete necrosis. These necrobiotic changes are indicated by a loss of the transverse and longitudinal striations; by a pycnosis or complete disappearance of the nuclei;

and by disintegration of the muscle substance into a structureless granular mass. Only the general contour of the fiber is preserved.

These areas of focal necrosis—for such they are—are surrounded by normal muscle fibers with excellently preserved striations and normal nuclei. Aside from the lesions described, the myocardium is normal in all respects.



Calcification of the Heart Muscle Fibers.

A point of importance is the absence of all inflammatory changes either in the areas of calcification themselves or elsewhere. In places there appears to be a slight proliferation of the nuclei of the perimysium about the calcareous fibers, and there may be found an occasional round cell. Of a true myocarditis, there is not a suggestion, and the lesion is distinctly not upon an inflammatory basis.

Whether there is a relation between the deposition of lime and a previous infiltration of fat, could not be determined in this case because the material was preserved in alcohol. There is however, no marked vacuolation of the fibers in the necrotic areas, nor did the appearance of the muscle in the gross suggest advanced fatty change. That there is no constant relationship between fatty degeneration of the heart muscle and calcification, is evident. The former is a most common, the latter amongst the rarest of findings. Hart has given consideration to this question. In his case, no fat could be demonstrated with Sudan in the calcareous fibers, although in the periphery of the necrotic areas, he found fibers showing considerable fatty change.

With potassium ferrocyanide and HCl, a few of the calcareous fibers take an intense blue color; the majority show only a diffuse bluish tinge. This finding is of interest in connection with the much debated question as to the relation between iron and calcification in the tissues. Hart[1] in his case, obtained a positive iron reaction in the calcified fibers, but ascribes no importance to his finding. Sumita[2] in his thorough work upon the relation of iron to calcification, also states that he obtained a positive reaction in calcified heart muscle. He gives no further details of his case, but his observation is important because he worked with iron-free reagents and took every precaution to avoid artefacts. The presence of iron in these cases is of interest since it is evidently not hematogenous in origin.

Of the histological changes in the other organs, we shall refer only to the deposits of lime found in the liver, adrenal tumor, lungs and kidney. In the liver, the lime was found in the form of granular masses in the walls of the abscesses. In the hypernephroma of the right adrenal, the tumor tissue was largely necrotic and infiltrated with pus. Here, as in the liver abscesses, lime was present in the suppurative foci. In the lungs, the lime was present in the form of globular or cylindrical masses of considerable size. These were situated either in the veins themselves—(old thrombi?)—or in the perivascular lymphatics. There was no calcification of the capillary walls or of the elastic fibers. In the kidney, several irregularly globular deposits of lime were found lying in the cysts beneath the capsule. There were also a few foci deeper in the cortex; in one place, the lime forms a cast lying within a Henle tubule. Most of the deposits are distinctly in the interstitial tissue.

In reviewing the reported cases of calcification of the heart muscle, we find that all authors agree that the deposition of lime is limited to the muscle fibers themselves, and to those only which show advanced degeneration. Fatty changes have been noted in the adjacent fibers (Roth,[3] Hedinger,[4] Wiechert,[5] Hart[1]), but not in those showing calcareous deposits. The collections of mono- and polynuclear cells which have been described about the calcareous areas, have been interpreted by a few writers as a primary myocarditis; more probably they represent a purely reactive inflammation about a calcareous foreign body, the lesion which precedes the deposition of the lime salts is a toxic necrosis of the muscle fibers.

The cause of the necrosis varies in the different cases. Hart's case was one of severe tertiary syphilis; Wiechert's, a case of paratyphoid A infection; Roth's a case of phlegmonous inflammation; in Askanazy's[6] case, there was an ulcerative endocarditis. Langerhans'[7] observation of a case of calcification of the heart muscle in association with chronic plumbism, shows that inorganic poisons may play a role. In our own case, the long continued suppurative pylephlebitis is the obvious cause for the toxic degeneration of the fibers.

We do not wish to discuss at length the broader problems concerned in the abnormal deposition of lime salts in the tissues. It is well known, since Virchow advanced his theory of calcium metastasis, that many cases of generalized deposits of lime in the different organs have been associated with destructive bone lesions—malignant growths, suppurative processes, and so forth. A typical case of this category is that recently reported by Tschistowitz and Kolessnikoff,[8] of multiple myeloma with extensive calcific deposits in the capillaries and elastic tissues of the lungs, in the glomeruli and membranae propriae of the kidneys, in the gastric mucosa, and in the media of various arteries. A similar case showing remarkable calcification of the endocardium of the left auricle, of the lungs and of the pulmonary veins, in a patient with myelogenous leukemia, has recently been reported by Verse[9] before the German Pathological Society. In cases of this sort the extensive halisteresis of the bones must be regarded as at least a contributory factor in the process. On the other hand, similar cases have been reported in which no destructive lesions of the bones could be demonstrated, and to which the idea of a "calcium metastasis" in Virchow's sense, does not apply. The experiments of Von Kossa[10] and of Rüdel[11] have shown that repeated injections of soluble calcium salts do not lead to calcification of the tissues.

On the other hand, there are many familiar examples of calcification associated with local necrosis of tissue, in which there is nothing pointing to an increased calcium content of the circulating blood, or to a failure in elimination. The calcareous incrustation of necrotic ganglion cells in the brain of general paresis is an illustration of calcification due to a purely local condition.

In the case here presented, there was no destructive bone lesion evident, although a complete examination of the bones could not be made. Furthermore, there is no reason to suppose on histological grounds that there was a failure on the part of the kidney or intestine to eliminate calcium properly, although only a chemical study of the excretions during life could have given us positive evidence of such an insufficiency.

All that we can say as regards the calcification of the heart muscle in this case is that it appears to be conditioned by a local necrosis of the muscle fibers; and for this local necrosis, we have sufficient cause in the long standing pylephlebitis. The necrosis is apparently of toxic origin and not due to infarction or to local myocarditis. The underlying cause for the calcific deposits in the lungs and kidney is less clear but in all probability they too are associated with similar local lesions of toxic origin. The lime deposit in the exudate of the chronic liver abscesses, needs no special comment.

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A CASE OF TUMOR OF THE PANCREAS.

RUSSELL L. CECIL, M.D.

Dr. Cecil presented a case of a tumor occurring in the pancreas of a male, aged 63, who came to autopsy at the Presbyterian Hospital on November 3, 1908. The anatomical diagnosis was adenocarcinoma of the ascending colon and chronic interstitial nephritis. The tumor of the pancreas was discovered quite by accident. Microscopically, the tumor was about the size of a pea, and was located near the surface of the pancreas. It was surrounded by a very narrow zone of pancreatic tissue, from which it was sharply defined.

Microscopically, the tumor was composed of masses of cells separated by a framework of connective tissue, which in many places was hyaline. The tumor cells were small, of a polyhedral shape, arranged in irregular cords. In some places the hyaline degeneration had involved the tumor cells. The supporting framework contained capillaries. The tumor was separated from the surrounding pancreatic tissue by a thin fibrous capsule.

Dr. Cecil said that the question arose whether the tumor originated from a duct, an acinus, or an island of Langerhans. From the appearance and arrangement of the cells he concluded that the tumor was an adenoma originating from an island of Langerhans. It was interesting to note that the islands of this pancreas showed the peculiar adenomatous hypertrophy, described by Reitmann, MacCallum, and others, which has generally been found in association with diabetes. There was, however, no record of a glycosuria in Dr. Cecil's case.

Discussion:

DR. W. G. MACCALLUM said that some time ago he had seen a case of almost exactly similar character described in some detail by Dr. Helmholz in the *Bulletin of the Johns Hopkins Hospital*. In that case, as in this, the nodule was regarded as an adenoma arising in the island of Langerhans, and it was thought that possibly it might act in some compensatory way for other islands of Langerhans. It had interested him especially, therefore, to hear what Dr. Cecil had had to say about the other islands of Langerhans in this particular pancreas. In another case in which there was diabetes the islands of Langerhans seemed more or less atrophied; but there were other islands, thought to be secondarily developed, to compensate for those which had atrophied.

Dr. Cecil, in closing the discussion, said that in addition to Dr. MacCallum's, Dr. Nicoll's case (the photographs of which showed the tumor to be almost identical with his) was the only other case he had seen reported.

A PRELIMINARY REPORT OF EIGHT CASES OF ADAMANTINOMA.

ELISE L'ESPERANCE, M.D.

The frequency of occurrence, the peculiarities in the histological structure, the difficulties in diagnosis, and the specific origin of various tumors of the jaw, now generally called adamantinomas, seem to demand greater attention than is commonly accorded them.

A brief résumé of our knowledge of these tumors may be permitted, preliminary to outlining the histological structure of several tumors of this class that have been studied in the Pathological Laboratory of Cornell University.

This interesting group of neoplasms was described by Magitot, one of the earliest observers (1875), as a cystoma or multilocular cyst of the jaw. The tumors were believed to have their origin from the surplus or retarded development of the teeth, this view being accepted by him as well as by Falkson, Eve, Bayer, and others of this period. Later Büchtmann (1881) assumed that they arise from the buccal mucous membrane, or the buccal mucous glands. The fact that they are derived from remnants of the enamel organ was first recognized by Malassez in 1885, and verified later by Kruse, Chibret, and others. On account of this origin they have frequently been called adenoma adamantinum.

The enamel organ is formed by an infolding of the ectodermal layer which caps the dental papilla. It is composed of a superficial layer of polyhedral cells, with an inner layer of high columnar epithelium, the adamantoblasts, between which lies a layer of highly peculiar reticular or stellate cells, the stratum mucosum.

The true adamantinoma, therefore, should show some features of these structures. Kruse based his conclusions on the fact that in his three cases he observed this typical structure of the enamel organ. Chibret's case also contained these types of epithelium.

Adamantinomas occur as cysts or solid new growths, either in the upper or lower jaw; according to some authors between the ages of six and twenty-five years, that is, at the time of the eruption of the teeth. But Massin has reported a case in a newborn infant, and Chibret one in a patient fifty-three years old. Our cases all developed in middle life, bearing no relation to the eruption of the teeth.

A considerable number of these tumors assume the form of simple or multilocular cysts, the so-called dentigerous cysts, excavating the alveolar process. Into these cysts papillary outgrowths occasionally develop and partially developed teeth have been found within them.

Adamantinomas are not malignant in that they do not form metastases (with the exception of one doubtful case reported by Eve in which he observed metastases in the lumbar lymph nodes and the suprarenals) but they infiltrate extensively the bony envelope, with atrophy of the osseous structure, sometimes splitting the bone.

They show, however, a strong tendency to recur locally, which was noted in several of our cases.

We have made a more or less arbitrary classification of these neoplasms, according to the type and arrangement of their epithelial cells, into three groups:

1. Acanthomatoid.
2. Plexiform.
3. Glandular.

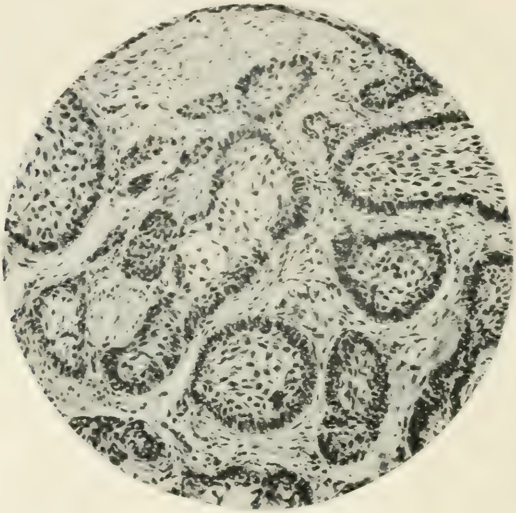


Figure I.

Between these types all degrees of variation exist. *The first group* shows the simple epithelioma composed of stratified squamous epithelium, in which many of the cells have undergone degeneration, in which condition they closely resemble the central cells of the enamel organ. The cellular elements are irregular, both in character and arrangement, many showing areas of hornification. In one specimen a single mass shows clear cells in one portion, undergoing hydropic degeneration, and in another contiguous area, typical hornified cells. I use the term hornified tentatively, as Borst has shown that endothelial cells undergo a hyaline degeneration, very closely resembling true hornification, which can be positively identified only by demonstrating the presence of striations, spines at the borders of the cells and kerato-hyalin granules. As I have not been able at the present time to show these characteristic features, I leave this for later study.

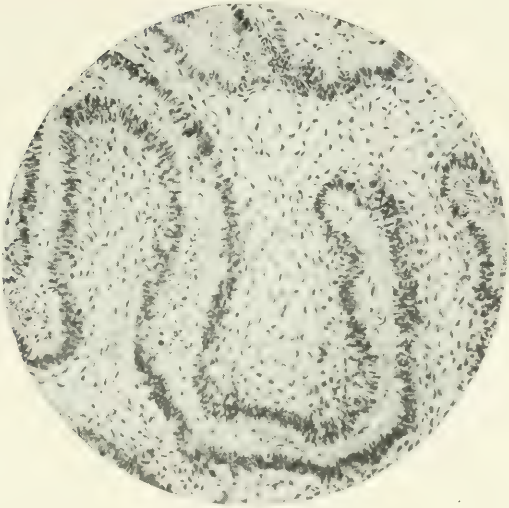


Figure II.

The second class comprises a type of tumor, in which the main portion is embryonal in character, and is composed of a fibrillar connective tissue stroma in which ramify convoluted masses of irregular epithelial cells.

These masses vary both in size and distribution, but as a rule closely resemble embryonal epithelium. Occasionally one observes areas that are composed of stratified squamous cells, developing pearls in the midst of this plexiform arrangement.

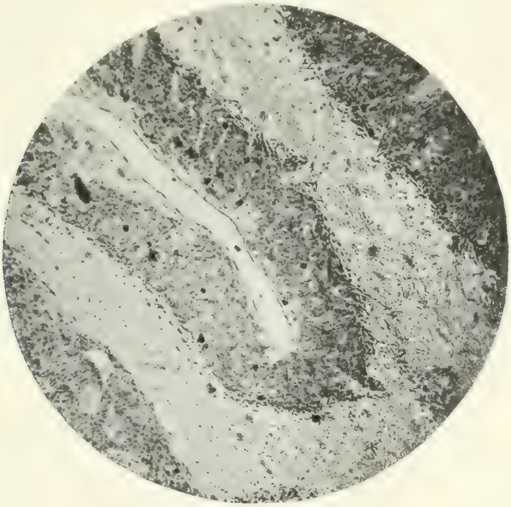


Figure III.

The third class is made up of large columnar epithelial cells arranged in rows or alveoli, producing a glandular structure. On cross section these rows appear to have a lumen, from the manner in which the cells surround the blood vessels. The existence of true lumina is doubtful. This type is apt to be vascular and show areas of hemorrhagic infarction.

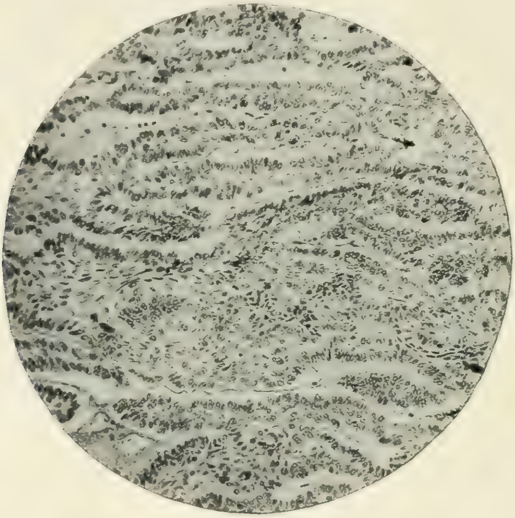


Figure IV.

In few other neoplasms does one see a more remarkable degree of metaplasia, than has been observed in the epithelial cells of a recurrent adamantinoma of this type, in which all variations were seen from the squamous epithelium of the simple epithelioma to spindle-shaped cells closely resembling spindle cell sarcoma, later assuming a diffuse round cell character, so similar to a round cell sarcoma that one would be in doubt concerning its true character without a knowledge of the clinical history and the previous specimens.

It is necessary therefore to differentiate adamantinomas not only from basal cell epitheliomas, for which they are sometimes mistaken, but also from spindle and round cell sarcomas, and a positive diagnosis, in some cases can be made only after careful study of the histological structure and clinical history.

Case I.—Acanthomatoid in type showing many resemblances to a simple epithelioma.

This tumor was scraped out of the tooth socket.

Case II.—Adamantinoma of the acanthomatoid type with groups of cells surrounding high columnar adamantoblasts.

Case III.—Adamantinoma resembling a simple epithelioma with high columnar cells, markedly reticular in center with one area showing cysts. A single mass in this tumor shows clear cells in one portion undergoing hydropic degeneration and an area of hornified cells.

Case IV.—Plexiform adamantinoma of the left ramus of the lower jaw. The clinical history is briefly:

Mr. M——, age thirty-seven years, admitted to St. Francis Hospital, November, 1910, in the service of Dr. Rogers, to whom I am indebted for the clinical history and material. The tumor was first noticed one year ago, growing slowly, to within the past month, when it began to increase very rapidly. The skin was adherent and of a bluish color over the site of the tumor, which appeared quite vascular, but not ulcerated. Microscopically the specimen shows the typical plexiform structure, masses of epithelial cells infiltrating the connective tissue. Many of these masses of epithelial cells show degenerated and necrotic areas. The outer layer shows columnar epithelium, gradually becoming cuboical until the cell outline is lost as they reach the necrotic portion.

Case V.—Glandular adamantinoma with plexiform arrangement. Shows many glandular characteristics. High columnar cells, enameloblasts and areas of hornified cells.

Case VI.—Glandular adamantinoma, marked glandular arrangement with peripheral layer of enameloblasts and spindle reticular cells in the center. Tumor recurred two years later, showing practically the same structure.

Clinical history: Mr. L——, age thirty-nine years, first noticed slight swelling of the gum and occasional bleeding after extraction of the first upper molar tooth in 1906. A few months later a small mass of tissue protruded from the tooth socket and was removed by a curette. About a year later, November, 1908, there was moderate thickening of the alveolar border and more bleeding tissue protruded from the socket. Section of a portion of this tissue showed the structure of a glandular adamantinoma. Partial resection of the superior maxilla revealed that the tumor had filled the antrum. On April, 1909, the tumor reappeared in the scar. Complete resection of the maxilla and pterygoid process of the sphenoid was attempted, but the patient died a few hours after the operation. The tumor had invaded the masseter muscle, the floor of the orbit, and the posterior wall of the pharynx. There was no involvement of the lymph nodes.

Case VII.—Glandular adamantinoma showing glandular arrangement with a typical layer of enameloblasts.

The next case is the most interesting of the series, and I shall give it in some detail.

Case VIII.—A recurring adamantinoma appearing as a plexiform epithelioma, recurring as a large alveolar and spindle cell tumor, and eventually as a round cell perithelioma.

Clinical history: Mrs. X——, forty-six years of age. In November, 1906, the removal of a molar tooth was followed by some inflammation of the maxilla, with a discharge of pus.

This was succeeded by a slight permanent swelling of the alveolar border. For one year there was slow enlargement of the gum. In December, 1907, there was frequent slight epistaxis. In May, 1908, a small tumor mass was found protruding into the inferior nasal passage, a portion of which on section was found to show the structure of a plexiform epithelioma. Resection of the superior maxilla was performed. The entire horizontal ramus of the jaw bone was much thickened, and the seat of a plexiform epithelioma which had eroded the dense portions of the bone and extended into the antrum. There was no involvement of the skin nor of the buccal mucosa.

In October, 1908, a recurrent nodule as large as a marble presenting on the mucous surface of the superior nares was removed and found to have the structure of a large alveolar and spindle cell sarcoma. A second nodule beneath the skin at the upper border of the malar bone was removed November, 1909. It had the structure of a large round cell perithelioma. A third recurrence in the same region, August, 1910, had the structure of a perithelioma or a diffuse round cell growth.

Discussion:

DR. JAMES EWING stated that he and his associates had been very much impressed with the frequency of occurrence and variety of structure of the tumors presented by Dr. L'Esperance, and on that account had thought it might interest others to see some of the specimens which had aroused this interest. Not only did these tumors occur with greater frequency than one might imagine, but they offered some very interesting observations on certain tumor processes. Especially in this last case the type of metaplasia had puzzled them a good deal. As a matter of fact, this tumor had been followed by them in New York and also by eminent pathologists in Boston, and some added interest was lent by a difference of opinion which had arisen as to the significance of the later tumors found in five operations. They were all agreed that the first two tumors were epitheliomas. As to the first specimen, however, they were not in accord as to its adamantinoma origin. When the third specimen arrived it was found to be composed of very small and indifferent cells. Dr. Mallory being out of town, another Boston pathologist pronounced it a spindle cell sarcoma. The fourth specimen caused much wonder as to whether they were really dealing with a tumor which had started with squamous cell epithelioma. Dr. Ewing felt compelled to maintain the position that the tumor had throughout been an epithelioma. The fifth specimen showed a diffuse round cell growth, which had no resemblance to any common form of epithelioma. They had to do here, he thought, with a degree of metaplasia which is extremely unusual, and an acquaintance with which is necessary if one is to be a safe diagnostician in this particular field.

Dr. E. Moschcowitz referred to a congenital epulis which he had studied a few months ago. The tumor at birth projected from the mouth, was the size of a walnut, and was attached by a pedicle to the incisor teeth. Microscopically, the tumor presented a picture totally different from any other that he had ever seen. It was composed of large polyhedral or elliptical cells between which were delicate bands of connective tissue. In one portion of the tumor there were epithelial inclusions. After careful study, Dr. Moschcowitz had come to the conclusion that the tumor had its origin in the papilla, and, more particularly, in the odontoblastic layer of the developing tooth, and that the epithelial structures were remains of the enamel organ. He had applied the term "odontoblastoma" to this tumor. The tumor was interesting in connection with those described by Dr. L'Esperance, inasmuch as it represented a growth from the connective tissue elements of the developing tooth, as opposed to the adamantinomas in which the epithelial origin is predominant. Dr. Moschcowitz thought that the case of Massin which Dr. L'Esperance had quoted as a congenital adamantinoma was a tumor similar in structure to his own. It was interesting to note that all the "odontoblastomas" thus far reported were congenital.

Dr. I. Levin asked whether there might not be a possibility that in these tumors one might find cells of varying natures in different parts of the specimen. He sought to explain the apparent change by saying that when a great number of sections of the same tissue are examined there might be enough variation in the cells of the different parts of the same growth to mislead one into the belief that they were sections of another tumor. He disagreed with the explanation given by Dr. Ewing, i. e., that there was a kind of metaplasia; and offered his as being the better explanation of the apparent change in the character of the tumor.

Dr. A. O. J. Kelly expressed himself as being entirely in accord with Dr. Ewing's views. He had seen many cases in the German Hospital, Philadelphia, which were similar to the one under discussion. Often, in his experience, he had found several records of the same specimen presenting conflicting diagnoses. On the whole, he felt quite confident that this was not to be attributed merely to an apparent change resulting from examinations of various sections of the same tumor (which was the theory advanced by Dr. Levin); but thought that the metaplasia must have occurred in a recurring growth of the tumor. Dr. Kelly had seen many cases which revealed many histological features, which one would never recognize, at first sight, as recurrences of a former tumor. He said, in addition, that the metaplasia found in recurring tumors of this kind was very extraordinary indeed.

ACUTE LYMPHATIC TUBERCULOSIS WITH PURPURA HEMORRHAGICA.

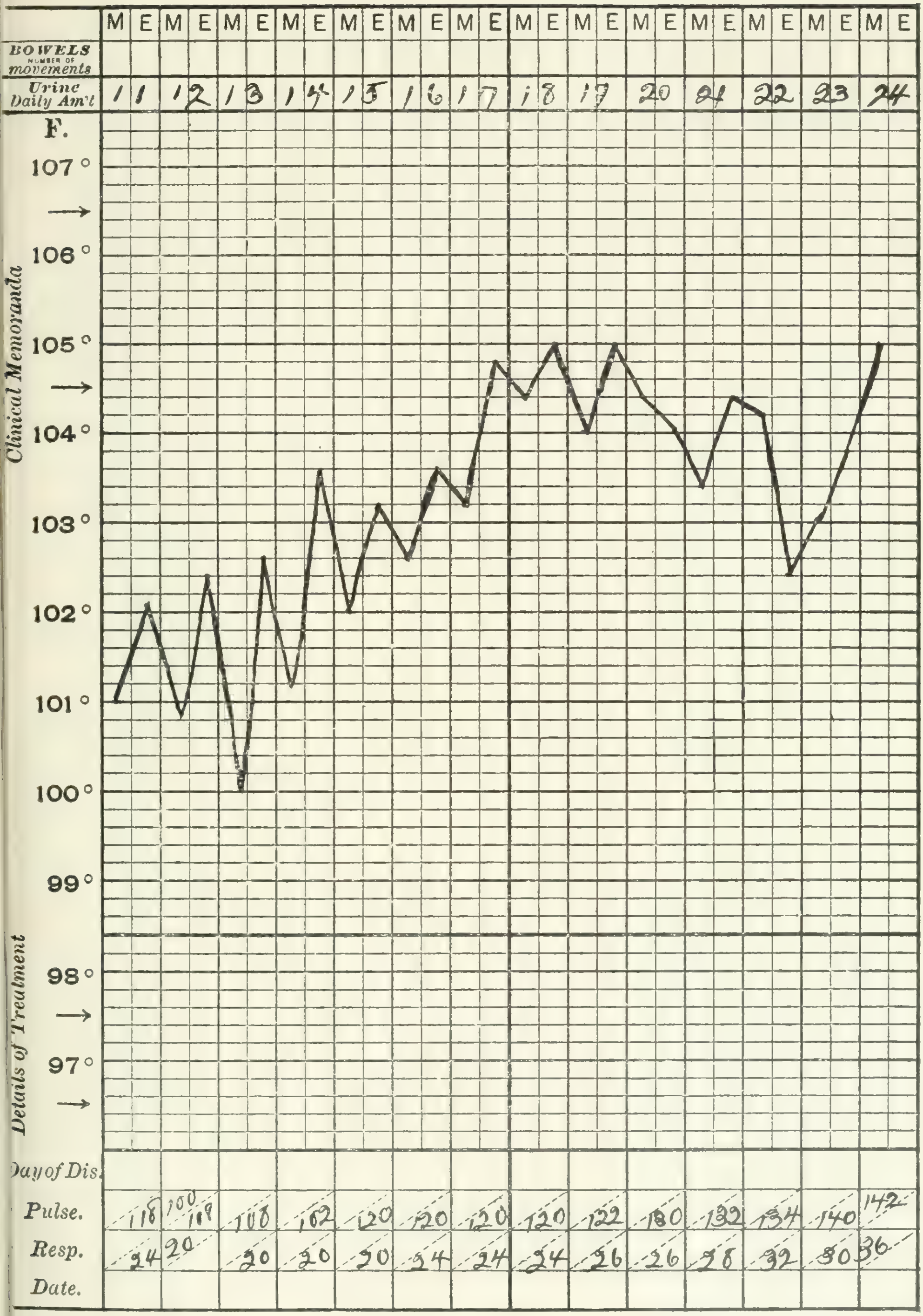
W. B. COLEY, M.D., AND JAMES EWING, M.D.

Mrs. P——, aged forty-two, married, four children, no family history of tuberculosis, no history of syphilis or cancer. Had always enjoyed vigorous health up to onset of present illness. About November 20, 1909, she noticed enlargement of cervical lymph nodes on both sides, principally posteriorly to the right sternomastoid muscle. The swollen nodes gradually increased in number and slowly in size, accompanied by some fever, anorexia, weakness, and loss of flesh. Early in December she had sore throat of moderate severity. Her husband states that there was some sore throat preliminary to the swelling of the cervical nodes. In December there were recurrent attacks of nausea and vomiting. About December 5 a hemorrhagic eruption appeared chiefly over the face, consisting of pin-point and broader superficial petechiæ most marked below the eyes. The eruption increased with the attacks of vomiting.

On admission to the hospital, in the service of Dr. Coley, she was weak but able to walk; T. 101-102° F., pulse, 118. The nodes on both sides of the neck, chiefly behind the sternomastoid muscle, were enlarged to the size of a bean or hickory nut, and several were found in front, but none in the axillae or groins. There was a marked hemorrhagic eruption on the face, and extending to neck, arms, and body were numerous minute petechiae. The spleen was slightly enlarged. There was no pain except from sore throat.

Blood examination (Ewing), December 13: Red cells, 2,480,000; hemoglobin, 70 per cent.; leucocytes, 5,500; mononuclears, 88 per cent.; polynuclears, 12 per cent.; eosinophiles, none. Culture on ordinary media negative. December 19: Red cells, 2,288,000; hemoglobin, 55 per cent.; leucocytes, 8,000; large non-granular mononuclears, 21 per cent; medium sized basophilic mononuclears, 63 per cent.; polynuclears, 16 per cent. Urine, highly colored, specific gravity 1,024, a trace of albumin, a few hyaline and granular casts, no sugar, heavy indican reaction. Culture from throat on blood serum yielded streptoccocci but no Klebs-Loeffler bacilli. A cervical lymph node above the clavicle was removed for histological examination. On December 13 the patient was seen in consultation with Dr. L. A. Conner, and the conclusion reached that the disease might be acute leukemia without leucocytosis, or acute Hodgkin's disease. Section of the lymph node later gave none of the specific signs of Hodgkin's granuloma, but showed the structure of a diffuse lymphoma or excessive inflammatory hyperplasia of large mononuclear cells with numerous mitoses. The sinuses, follicles, and cords were obliterated, and it was impossible to distinguish the lesion from a leukemic process.

The condition of the patient grew rapidly worse, the temperature rose to 104-106° F., by December 17, and remained at that level without definite remission. The vomiting recurred. The eruption became diffuse and innumerable fine and large petechiae appeared over limbs and body. The arms were completely covered by successive crops of petechiae, at first brilliant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red, later becoming brownish. December 19 blood culture was again negative. There were no hemorrhages from the mucous membranes. The patient passed into a state of semi-coma, which persisted for several days until her death, December 24, at 12.30 p. m.

Report of post-mortem examination, December 24, 1909, four hours after death, by Dr. Ewing:

Body of a large, well-nourished woman. No rigor; no edema. There is a profuse, universal hemorrhagic eruption of the skin, consisting of minute points becoming confluent, forming flat petechiae in many places, especially on arms, and diffuse all over face. Some points are recent and bright red, others of longer duration and slightly brownish. The buccal mucosa shows a few medium sized petechiae. Lymph nodes of neck are moderately enlarged, firm; those in axillae and groins slightly enlarged.

Heart, normal; right chamber filled with dark fluid blood.

Lungs—There is a partial consolidation of posterior portions of both lungs. Section is very deep red, intensely congested, and shows minute hemorrhages and areas of consolidation as of lobar pneumonia. Bronchi intensely congested; no signs of tuberculosis.

Pleura shows a thin layer of fresh fibrin and many petechiae.

Liver—Size and consistence normal. Surface shows a few subserous hemorrhages. Surface and section show many whitish foci, miliary to the size of a pea, as of irregular tubercles. Parenchyma deeply congested, markings obscure.

Spleen—Moderately enlarged, 14 x 8 x 5 cm., firm, pulp grayish red, follicles visible as minute gray points.

Pancreas—Normal.

Peritoneum—Shiny, normal, except for a few small petechiae.

Stomach—Mucosa distinctly thickened, the folds being unusually high; but no enlarged follicles are visible. It shows some small hemorrhages. Small intestine not examined.

Colon—Shows uniform swelling of all solitary follicles, a very few of which show superficial erosions.

Pelvic Organs—Normal.

Kidneys—Capsules are mottled with many small hemorrhages. Section shows cloudy swelling with intense congestion of medulla.

Lymph Nodes—The bronchial, thoracic, retroperitoneal, and mesenteric lymph nodes are enlarged, soft, intensely congested, with small hemorrhages, and show many miliary to pea-sized grayish areas resembling tubercles. The largest nodes are the thoracic, which measure 1-3 cm. in length. They are softer and more acutely inflamed than ordinary tuberculous lymph nodes.

Anatomical Diagnosis—Subacute granuloma of lymph nodes, probably tuberculous; tuberculosis of liver; acute exudative pneumonia. Miliary and diffuse hemorrhages of skin, serous membranes, and renal capsules. Diffuse hyperplasia of lymphatic system of stomach, colon, cervical, thoracic, abdominal and axillary nodes; pharyngitis.

Microscopical Examination—Lymph node of neck removed at operation. Section shows diffuse hyperplasia of large mononuclear cells with vesicular nuclei, obliteration of sinuses, cords and follicles. There are no tubercles or necrosis. There are some mononuclear giant-cells. There are many mitoses. Thoracic and abdominal lymph nodes show intense congestion. The tubercles show liquefaction rather than caseous necrosis. They are surrounded by very many phagocytic cells containing ten to fifty englobed leucocytes. The nodes show diffuse hyperplasia of mononuclear cells similar to that described above. Stains for tubercle bacilli revealed a very few elongated strongly acid-fast bacilli resembling tubercle bacilli; they were found only in the necrotic foci.

Liver—There is general granular degeneration of the liver cells with intense congestion. The portal canals are infiltrated with a thick mantle of large mononuclear cells. The tubercles visible in the gross include the portal canals and a few show liquefaction necrosis. Here a few strongly acid and alcohol-fast bacilli are found resembling tubercle bacilli.

Spleen—There is diffuse hyperplasia of large mononuclear cells obliterating cords and sinuses and encroaching upon the follicles.

Kidneys—There is diffuse granular degeneration of the tubule cells. Many miliary lymphomata are scattered throughout the cortex and medulla.

Stomach and Colon—In the mucosa there is marked hyperplasia of solitary follicles, many of which are the seat of superficial ulcers.

The bone marrow in the vertebral bodies is intensely congested and the sinuses are gorged or ruptured. There is a feeble hyperplasia of large mononuclear cells. Islands of nucleated red cells are missing, and the marrow cords are obliterated.

Diagnosis—Subacute lymphadenitis and hepatitis due to infection by tubercle or tubercle-like organisms. Hyperplasia of lymphatic system. Miliary lymphomata of kidney. Exudative pneumonia.

Bacteriological Study—By Dr. Ewing and Dr. Frank M. Huntoon.

Cultures of retroperitoneal lymph node on glycerin egg medium, made December 24, gave a slight growth of an acid-fast bacillus resembling the tubercle bacillus, first seen on February 11. All other cultures negative. Of five monkeys inoculated intravenously on December 28 with emulsion of lymph nodes, three died in a few days of gastroenteritis, one of general tuberculosis on February 3.

The fifth monkey died on April 11, of general tuberculosis, most marked in the omentum and liver, with oldest lesions in the inguinal lymph nodes at the point of inoculation. A sixth monkey inoculated with 5 c.c. of blood serum drawn December 19, died March 24 of general tuberculosis very abundant in the lungs, liver and spleen. Five guinea pigs and four rabbits were inoculated with lymph node emulsion intraperitoneally or intravenously. One guinea pig, inoculated December 28, died February 28 from tuberculosis of mesenteric vessels due to a single large granulomatous mass in mesentery. No tubercle bacilli were found in this mass and cultures were negative. The mass consisted of inflamed lymph nodes, showing lymphoid hyperplasia, edema, but no necrosis. Of two guinea pigs inoculated on January 25 with 2.5 c.c. emulsion of liver which had been kept on ice, one died on March 6, of general tuberculosis. From the spleen a pure culture of tubercle was obtained.

Four rabbits were inoculated intravenously with 0.5 c.c. of emulsion of lymph node. They failed to show any external sign of disease at the end of six months.

The foregoing case presents several remarkable features, and in some respects is unique. Tuberculosis running an acute course of six weeks, with continuous fever, universal hemorrhagic eruption, systematic involvement of lymphatic organs, bacteremia, and absence of specific lesions in the lungs, is a clinical type of the disease not described in current text-books of medicine, and so far as we can learn not previously observed.

The most notable feature of the case is the limitation of the disease chiefly to the lymphatic system, that tissue which ordinarily possesses a relative immunity to this infection. The earliest lesions were those of the cervical lymph nodes from which the infection spread through the mediastinal and abdominal nodes, eventually producing multiple miliary lesions of the liver and spleen. In addition to the focal lesions in which tubercle bacilli were abundant, there was a diffuse hyperplasia of the lymphatic structures of the stomach and intestinal tract. The bone marrow showed a draining of leucocytes with occasional focal hyperplasia. In the liver there was extensive lymphoid infiltration of the portal canals without demonstrable bacilli, and numerous larger necrotic lesions in which bacilli were present.

The histological structure of the necrotic lesions containing bacilli was peculiar. These lesions were of acute exudative and hemorrhagic character ending in central necrosis. They contained giant macrophages inclosing twenty to fifty lymphocytes, and were quite different from any cells seen in ordinary tuberculosis. In the lymphomatous areas not containing bacilli, in the cervical node removed during life, in the portal canals, and in the wall of the stomach and colon, the lesions were indistinguishable from those found in many cases of lymphatic leukemia. The pneumonia was a terminal process which the clinical signs indicated as of a few days duration. It was, however, at least partly of tuberculous nature, streptococci being abundant and tubercle bacilli being present in small numbers in a few areas of necrotic bronchitis.

The blood picture suggested the diagnosis of acute leukemia. There was marked relative and slight absolute lymphocytosis. Many of the lymphocytes were of very large size with large nuclei. In the smaller cells azure granules were abundant. Blood examinations have been reported in several cases of tuberculous purpura, all of which showed little or no leucocytosis but excess of polynuclear cells. The striking relative lymphocytosis of the present case is therefore an exception to the rule. The suspicion of leukemia was strengthened by the structure of the cervical node removed on December 13, which could not be distinguished from a leukemic process. The anemia and the hemorrhagic eruption also encouraged the belief in the leukemic nature of the disease, and it was this belief that led to the inoculation of several monkeys. The association of tuberculosis with lymphatic leukemia is so commonly observed as to lead to the suspicion that lymphatic leukemia may sometimes be of tuberculous origin. The present case, especially the structure of the cervical lymph nodes, the widespread lymphoid hyperplasia, the lesions of the liver, and the blood picture, lends some support to this view.

The distribution of tubercle bacilli was peculiar. They were found only in the necrotic areas, but not in any of the extensive areas of lymphoid infiltration. The results showed that they were present in the circulating blood. While cultures of the blood on ordinary media were negative, inoculation of 5 c.c. of the blood drawn December 13 into the superficial vein of the groin of a Rhesus monkey was followed by the death of the animal in three months with acute general tuberculosis and a human tubercle bacillus was isolated from the organs by culture. We believe that intercurrent tuberculous infection of our monkeys can be eliminated. They were all recently imported, and three of the lot that died from enteritis within a few days of their receipt were entirely free from tuberculosis.

In morphology the bacilli were unusually long, and many much elongated and numerous branching forms were seen in sections. Since these branching forms stained with methylene blue they were at first regarded as streptothrix. They were, however, strongly acid-fast. An intensified Gram stain, as used by Much, gave more bacilli than carbol-fuchsin, but not in any new situations. In the lymphomatous areas it was not possible to find any Gram-positive granules that might be identified as derivatives of tubercle bacilli. The bacillus proved to be of the human variety, on morphology, because of its strongly acid-fast properties and its long, beaded and branching form; on cultural characters, as it grew luxuriantly on egg medium, produced a pellicle on broth in about three weeks, and the culture on egg developed a distinct pink color; and on biological features, failing to kill rabbits in six months, frequently proving fatal to guinea pigs, and causing acute general tuberculosis in Rhesus monkeys. Its acid production has not yet been determined.

The most striking clinical feature of the case was the extensive purpura which appeared shortly after the first symptoms and persisted with increasing intensity until the termination of the disease. Yet the occurrence of extensive purpuric eruptions in the course of tuberculosis has long been recognized, although in current text-books its importance is much underestimated. Thus Bensaude and Rivet, in 1906, gave a very full account of the relation of purpura and tuberculosis, drawing extensively from journals and text-books of fifty years ago; but in Osler's System, in an otherwise able review of purpura, the reader draws the impression that tuberculosis is practically a negligible factor in the etiology of purpura.

Bensaude and Rivet state that general purpuric eruptions occur, *first*, as a premonitory symptom of tuberculosis; *second*, in the course of acute or chronic tuberculosis; *third* in latent pulmonary tuberculosis; and *fourth*, with extrapulmonary lesions.

There is an extensive literature on the subject of tuberculous purpura, illustrating all of these relations.

(a) The premonitory form is well illustrated by a case of Mollière's, a man of twenty years, without tuberculous antecedents, who suffered for six weeks from joint pains and general purpura, before the appearance of cough, hemoptysis, and progressive pulmonary lesions ending in death one month later. Very similar cases are reported by Cohn, Wiechel, and Moizard and Grenet, the afebrile purpura preceding by one or two weeks, an acute pulmonary phthisis. In a case of Carnot and Harvier severe purpura of three weeks' duration disappeared and the patient seemed well, when pulmonary signs suddenly developed and cavities formed in six weeks. In a case reported by Hoke, a woman of fifty-nine years, previously quite well, suddenly developed a universal punctiform and macular purpura without fever. Two weeks later she died suddenly from cerebral hemorrhage. Autopsy showed acute miliary tuberculosis of the kidney and pelvic lymph nodes. In Herzog's case, a boy, whose parents were tuberculous, began to have attacks of purpura at four and one-half years of age, which were frequently repeated during seven years, when in his eleventh year he developed acute pulmonary phthisis which was rapidly fatal.

(b) In the majority of cases the purpura has marked a severe or fatal exacerbation of pulmonary tuberculosis, as reported by Bensaude and Rivet, Wagner, Bauer, Pratt, and others. In Pratt's case, a sailor, twenty-five years of age, duration of disease three months, general and increasing purpura hemorrhagica existed during the last seven weeks. Besides a general tuberculosis of lungs and spleen, with gastric ulcers, there was marked enlargement and caseation of many lymph nodes throughout the body.

(c) The relation to latent tuberculosis is illustrated by a case of Dumas', of a soldier who suffered from punctiform purpura for several days and then suddenly died from cerebral hemorrhage. Autopsy revealed old tuberculous pleurisy and peritonitis. In many of the premonitory cases there is doubtless a latent focus which serves as a source of general infection, as in several cases collected by Bensaude and Rivet, and Carnot and Harvier.

(d) Purpura hemorrhagica has occurred in the course of many extrapulmonary lesions, as in the following cases quoted mostly from Bensaude and Rivet. With acute tuberculous meningitis (Troisier, 1873); in tuberculous orchitis (Gossner); tuberculosis of kidney and pelvic lymph nodes (Hoke); with tuberculous mesenteric nodes (Achmeticew); or cervical nodes (Kissel); or bronchial nodes; and with chronic coxitis (Fox). In a case of Vollbracht's, eleven months after a severe purpura, signs of Addison's disease appeared and autopsy showed tuberculosis of the adrenals.

It thus appears that severe general hemorrhagic purpura occurs under many conditions in connection with tuberculosis, and that it usually indicates an exacerbation of the tuberculous process. While ranking among the relatively rare manifestations of the disease its occurrence is sufficiently frequent to deserve more attention than it receives in current literature.

Many theories have been suggested for the pathogenesis of tuberculous purpura, from a constitutional hemorrhagic diathesis to acute bacteremia.

Although Rosenberger's results of finding bacilli in the blood in all of 125 cases of tuberculosis have not been verified, it has been fully proven by many observers that tubercle bacillemia is very common. The infectivity of the blood was shown by Veuillemin in 1866, and Weichselbaum found bacilli in the cadaver blood of several cases. In 1905 Jousset, by inoscopy, demonstrated tubercle bacilli in the blood in eleven of thirty-five cases (31 per cent) of acute and chronic phthisis. Liebermeister often found tubercle bacilli in the blood in pulmonary phthisis, and showed that this bacillemia is not of unfavorable prognosis since it is not often followed by general miliary tuberculosis. Recently, 1910, Jessen and Rabinowitsch found bacilli or Much's granules in the antiformin sediment of nine out of thirty-six cases of tuberculosis, and they agree with Liebermeister that it is not of unfavorable prognosis. In view of these observations it would not be unreasonable to assume that tuberculous purpura is associated with sudden access of tubercle bacilli into the blood stream. Yet the occurrence of purpura in so many cases in which no general tuberculosis followed repeated attacks, and its complete disappearance, as in Gossner's case after extirpation of a tuberculous testicle, and the peculiar distribution of the petechiae in many cases, indicate that the lesions result chiefly from the action of toxic substances produced in the course of the disease. In the present case the histology of the petechiae showed nothing suggestive of the presence of bacilli.

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PRESENTATION OF A CASE OF CYSTICERCUS CELLULOSAE (?) OF THE FOURTH VENTRICLE.

CHARLES NORRIS, M.D.

The case was that of an Italian of thirty-five years. Since his immigration to this country, five years ago, he had always lived in New York City. Two months before his admission to Bellevue Hospital, in the service of Dr. James Alexander Miller, to whom I am indebted for the clinical history, he began to vomit after meals, the vomiting becoming more constant; and headaches set in, which became more and more severe. On admission the patient was fairly well nourished; there was constant vomiting and severe headache. Ophthalmic examination of the left eye showed a choked disc. The other eye examination was unsatisfactory. He was reported by the orderly to have died suddenly, several days after admission.

At autopsy, the convolutions of the brain were found markedly flattened, and with considerable distention of the cisternae at the base. The lateral and third ventricles were distended with clear fluid. On opening the roof of the fourth ventricle, a group of vesicles, composed of three cysts, the largest 5 x 7 mm., was found attached by a delicate pedicle to the wall of the fourth ventricle in its upper and lateral portion near the iter. There was considerable thickening of the ependyma of the iter and marked proliferation of the pia in the lateral processes of the fourth ventricle. A long worm, which was identified as *Tænia solium*, was found in the jejunum. No other noteworthy lesions except a chronic gastritis were found.

It is conceded that *Tænia solium* is the worm which infects man with cysticercus. The portal of entry is the intestine, as in this case. The ripe eggs entering the stomach during the regurgitation following vomiting (or a segment of the worm itself) are dissolved by the gastric juice, and the worm is set free from its shell and then penetrates the wall of the stomach. This mode of "auto-infection" of the worm was thought by Bruns to be the usual way in which a human being was infected. In only four of the seventy-two cases of cysticercus in the fourth ventricle, reported by Stern,[1] was a worm found in the intestine. Virchow, and practically all other authorities, believed that the infection occurs through the ingestion of uncooked meat or unwashed salads, etc. Owing to the habit of eating uncooked meat, the so-called "Finnen-krankheit" was very prevalent in Germany, before the meat inspection laws were in force.

Virchow reported that before 1885 one out of thirty-one bodies was infected by cysticercus. Henneberg's statistics (1903), compiled since the inspection laws were enforced, found the percentage of infected cadavers to be only 0.16 per cent. in Berlin.

The most interesting feature about the cysticercus disease of the fourth ventricle is the clinical history. The symptoms that are almost invariably present are headache, vertigo, and vomiting.

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[1] Ueber Cysticerken im vierten Ventrikel. Arthur Stern. *Zeitschrift für klin. Medizin.* Bd. 61, 1907, pp. 64-121.

In 11 per cent. of the cases collected by Stern there were no symptoms. The disease has usually been diagnosed as tumor or hysteria, on account of the intermittent character of the symptoms. The cardinal point of diagnosis is that described by Bruns (1902), viz., the relationship of attacks of dizziness and of sudden death to sudden movements of the head.

The case was reported before sections of the cyst and its absolute identification had been made.

Dr. Norris also called attention to a second case, a gross specimen from a man sixty-seven years of age showing a tumor of the pituitary gland, probably an adenoma, without acromegaly.

Discussion:

Dr. J. H. Larkin said that at one of the meetings of the Society last year he had presented a very remarkable specimen of cysticercus of the brain. It should be remembered, however, that a great many of the cases of cysticercus cellulosæ of the brain were accidental findings, and that no diagnostic or prediagnostic condition had been discovered. Bruns, in an article which is one of the best on the subject, had gone into some detail as regarded the diagnostic or pre-diagnostic condition of the individuals who might have a predisposition to such an infection. Dr. Larkin said further that cysticercus of the brain was generally in the fourth ventricle, and that the dilatation might reach an enormous size. The specimen to which he referred was ten or even fifteen times as large as the one presented by Dr. Norris, They were of identical morphological type, i. e., three or four cysts closely connected by a small pedicle. The great majority of cases (in fact all of those reported by Bruns, and Dr. Larkin's) had been cases of sudden death. Dr. Larkin had also presented at the meeting referred to the brain of a monkey dying from cysticercus cellulosæ. In the monkey, the cysts were generally scattered throughout the cortical substance, and were not found in the cavities of the brain.

Dr. Coplin spoke of a similar case, reported by Dr. Lloyd. He had not reviewed his notes, and remembered merely the more striking features. He recalled the fact that there were a large number of cysts in one of the lateral ventricles and a few collapsed sacs. The patient, who was said to have had some mental defect, maintained that with movements of his head he could feel things move about within. At autopsy it became evident at once that in the dilated ventricle not fully occupied by the cysts they might have floated forward or backward, and that the sensation complained of by the patient was in harmony with the anatomic findings. Dr. Coplin also recalled that there was considerable distention of the ventricles, together with very marked flattening of the convolutions, due, of course, to the distention. He did not remember, however, whether death had been sudden, or whether there were any other pathological findings of note.

Dr. H. W. Cattell said that he had had among his series of autopsies one case of cysticercus cellulosæ of the brain (1897). The death was sudden and the case was brought to the coroner's office as one of hydrophobia, the man having been bitten by a dog six weeks previously, the dog, however, presenting no signs of rabies. Briefly, the history was that of a man, aged twenty-three years, the autopsy revealing marked edema of the lungs and throat induced by chronic nephritis and cardiac failure. The brain was edematous and showed the presence of a number of cysticerci cellulosæ in a good state of preservation. The majority of these cysts were found in the sulci in the neighborhood of the larger blood vessels derived from the anterior, middle, and posterior cerebral arteries, while a few of the smaller ones were embedded in the brain substance, thus showing a wide distribution. No cysts were found in the ventricles. The man was a German, both by birth and in his manner of living. Dr. Coplin had reported from an examination of the medulla and cord that these parts did not show any evidence of hydrophobia.

A TUMOR OF THE NECK, SHOWING UNUSUAL HISTOLOGICAL FEATURES.

J. E. WELCH, M.D.

Case History: A. B. Confinement No. 17762. Age thirty-two; born in Ireland, Para 5; admitted to hospital May 20, 1910, presenting a condition of paraplegia and swelling on the right side of the neck. History as given by the patient was as follows:

During the latter part of a previous pregnancy, which was two years before admission, she noticed a small painless swelling on the right side of the neck, which varied in size from time to time, but was never tender. After the birth of this child, the swelling for a time grew much smaller, and then later increased gradually over a period of about one year, when she became pregnant again. During this last pregnancy the enlargement grew steadily until the time of death. About the middle of February, 1910, the patient was seen by Dr. Adolph Reich in her home. Dr. Reich gives an account of having found the patient at this time sitting in a Morris chair and unable to use her legs in any way. The history was not gone into carefully at this time, but the patient said she had been confined to her chair for several weeks, being unable to lie down on account of substernal pain, which always came when she assumed a reclining position. At this time she was about five and a half months pregnant. She was later advised to enter the hospital, which she did May 20, 1910. On admission to the Lying-In Hospital she was found to be between eight and nine months pregnant, appeared anemic and presented a tumor on the right side of her neck about the size of a hen's egg. Blood count on the day following admission showed 3,880,000 red cells, hemoglobin 78 per cent., 11,600 leucocytes, and a differential count as follows:

Small lymphocytes..........	10.	per cent.
Large lymphocytes..........	1.5	per cent.
Polynuclears	88.	per cent.
Eosinophiles	0.	per cent.
Transitionals	.5	per cent.

Urine analysis on this same date showed the following: Acid, deep amber, specific gravity 1,105, trace of albumin, trace of acetone, urea 0.9 per cent., no excess of indican; few pus cells and epithelium.

On May 24 the leucocyte count was as follows:

Total number of leucocytes.........	12,000	
Small lymphocytes..........	5.	per cent.
Large lymphocytes..........	4.5	per cent.
Polynuclears	89.	per cent.
Eosinophiles	1.5	per cent.

For the first five days after admission the patient's temperature was in the neighborhood of 100 ; on the sixth day she had a chill and her temperature rose to 105°; on the seventh day she was delivered of a premature child. From that time on until death her temperature fluctuated between 104° and 100°, several times reaching 105°. Two days just preceding death her temperature was subnormal, below 96°.

The question that presented itself to the surgeon in charge of this case was the possibility of relieving the paraplegia by laminectomy and removal of the growth from the spinal canal. The inference was that this pressure was due to a secondary deposit from what was considered the primary growth in the neck, which was thought to be lymphosarcoma, tuberculous adenitis, or Hodgkin's disease. In order to determine its exact nature, several laboratory tests were applied as follows.

Having first in mind lymphosarcoma, the Crile hemolysis test was made but proved negative; the von Pirquet test was then applied twice and proved negative both times. At this time the sputum was also examined, but no tubercle bacilli were found. Lastly, a Wassermann reaction was tried with a negative result.

At this time it was decided to remove under cocaine a small piece of the enlarged gland. This was done, and the specimen was sent to the laboratory for diagnosis. Microscopic sections of this tissue showed a lymphatic structure surrounded by a normal fibrous capsule. The lymph follicles in the central part of the tissue showed hyperplasia of the lymphoid cells. Towards the periphery of the gland there was an extensive formation of very dense hyaline interstitial fibrous tissue. This was especially marked beneath the capsule and was less dense as the center of the node was approached. The section appeared to present a simple inflammatory condition. Not being satisfied with this report, another piece of the tumor was asked for and received a few days later. Sections through this tissue showed changes as above described, i. e., extensive formation of interstitial hyaline fibrous tissue peripherally and lymphoid hyperplasia centrally. The lymph cells showed no tendency whatever to penetrate the capsule, but, instead, where this process might be expected, a fibrous condition was found. This second specimen showed, however, in addition, scattered through the hyperplastic lymph follicles a few giant cells having large oval nuclei placed centrally and rather small cell bodies. The association of these peculiar giant cells in the hyperplastic lymphoid follicles with a tendency to form interstitial fibrous tissues at the periphery of the gland led to the deduction that the process was an inflammatory one and of the nature of a granuloma, hence the diagnosis of Hodgkin's disease was made. After removal of the sections for microscopical examination, the patient's condition grew gradually worse, the anemia increasing, and the tumor in the neck enlarging. About three months before the patient died, a small tumor appeared on the left side of the neck, but did not grow very large.

Post-mortem examination (made by Dr. Douglas Symmers) —Inspection shows the body of a woman, poorly nourished, skin and visible mucous membranes very pale; on the right side of the neck a tumor mass measuring about 1 cm. in length and 3 cm. in breadth, with its long axis running parallel with the long axis of the neck. The mass is coarsely lobulated, slightly movable against the deeper structures, but attached to the skin. Over the lower part of the tumor is a small surgical scar well healed. The supraclavicular lymph nodes are palpable. The axillary, epitrochlear, and inguinal nodes can not be felt. The lower limbs are flexed at the knees at an angle of 135° and can be straightened only with difficulty. Both heels present blackened decubital ulcers. The post-tibial tissues at the lower third of the leg are markedly edematous. In the sacral region is an enormous irregularly outlined decubital ulcer. The edges are thickened and the base is made up of underlying bony tissue which is discolored and ill-smelling. Several bony prominences, including the posterior spine of the ischium and the head of the left femur are freely exposed.

Brain—On removing the dura mater, a minute rounded metastasis on the right side comes into view. The brain is small, sulci are deep, convolutions are narrow and atrophic. On section, no noteworthy appearances are observed.

Spinal Cord—On opening the medullary canal, a collar of tissue corresponding in all naked eye essentials to that described in the neck and abdominal lymph node comes into view around the mid-dorsal cord, between the sixth and eighth dorsal vertebrae. On removing the cord and opening the meninges, this tumor mass is found to be entirely extradural. The underlying cord, however, is small and shows evidences of compression. On section the mid-zone of the cervical cord on either side presents considerable brick dust discoloration. In the dorsal cord no definite changes are visible to the naked eye.

Thorax—The thymus is absent; diaphragm normally placed; dense adhesions posteriorly in both pleural cavities; pericardium is normal; the heart is small, brownish yellow in color and flabby, shows no special pathological change. The lungs show moderate emphysema only. Immediately beneath the pleura near the hilum of the left lung is a small flattened pale mass which, upon section, presents a pale, smooth, rather translucent appearance. It extends downward into the parenchyma for a short distance. On removing the tongue, larynx, thyroid and upper esophagus, the tumor mass previously described on the right side of the neck is partly dissected out and removed. It appears to spring from the regional lymph nodes and to bear no connection with the periosteum of the jaw or spine. It fills in the neck from the level of the skull almost to the clavicle and lies close to the side of the spine. It is made up on section of innumerable rounded or oval bodies which are firmly bound together, and present a perfectly smooth, pale, translucent, glistening surface, the substance of which is firm in consistency. Occasionally yellowish, apparently necrotic areas are present in the cut surface.

Spleen—Is considerably enlarged, and the capsule is tense; it has a diffuse steel-blue color. Close inspection of the cut surface shows numerous areas of amyloid degeneration.

Liver—Is greatly enlarged; lower border of the right lobe reaches the level of the umbilicus. This organ is yellowish in color, the surface is smooth, lobules are well differentiated; no focal lesions or amyloid are found.

Pancreas—Unchanged.

Adrenals—Unchanged.

Kidneys—Left, surrounded by considerable fat; on section the organ cuts readily. Capsule strips readily, leaves behind a surface which in places is greyish red and smooth, but in other places is studded with pin-head to bean sized, cream colored bodies which release soft pus when the capsule is reflected from them. The cortex is, for the most part, very pale, bulges greatly beyond the cut edge of the capsule, and is poorly differentiated from the medulla. Scattered through the cortex and medulla of the lower third of the organ are innumerable points and streaks made up of pus. The mucous membrane of the pelvis is swollen, pale, and opaque. The right kidney is essentially like the left.

Bladder—Small; walls are greatly thickened; mucosa is diffusely reddish, very opaque, and markedly swollen and edematous. At one point is a small collection of pus lying immediately beneath the surface.

Uterus—Shows no changes.

Gastrointestinal Tract—Shows no lesions.

Peritoneum—Shows no change.

Abdominal Lymph Nodes—At the lower end of the spine on the left side near the sacro-iliac synchondrosis are numbers of enlarged lymph nodes which upon section present essentially the same naked eye appearances as those described in the neck, but with the addition of numerous minute reddish points in the cut surface.

Microscopic sections through the primary tumor in the neck, the nodule in the lung, and the growth in the spinal canal, all show a similar structure which is very different from the picture presented by the sections examined ante-mortem. There is a very extensive production of fibrous tissue which is very dense, has a hyaline appearance for the most part, and has a retiform arrangement through the growths. The interstices of this fibrous tissue framework contain a very great variety of cells. There are numerous very large multinuclear and uninuclear giant cells. None of these giant cells resemble in any way those found associated with tuberculosis or syphilitic lesions. Their nuclei are not arranged peripherally, but are found in the center of the cells, usually overlapping each other and occasionally having a roseate appearance. There are also found numerous very large cells with dense protoplasm staining deeply by eosin with dense chromatin nuclei, many of which show mitotic figures. There are a few plasma cells scattered here and there, and an occasional eosinophile. The lymphoid tissue has been almost entirely replaced. A few cells only remain to indicate its former presence. Superficial examination of these tumors might lead to the conclusion that the growth was sarcomatous, but consideration of the ante-mortem histological appearance and the tendency to fibrous tissue proliferation rather than new cell formation, inclines one to the conclusion that the process belongs to the class of granulomata. This conclusion is also favored clinically by the long duration of the disease, and the lack of a tendency rapidly to infiltrate surrounding structures which is one of the marked characteristics of sarcoma. Microscopically, we find everywhere marked tendency to the production of interstitial hyaline fibrous tissue, which is true especially about the periphery of the growths, a situation where in sarcoma we expect to find a very cellular structure instead of a fibrous one.

I wish to present this as a case of Hodgkin's disease with unusual histological changes late in the disease.

	Average Count in All Cases of Dr. Reed.	*Average of Three Counts in This Case.*
Red blood cells	3,829,000	3,890,000
Hemoglobin ......Per Cent.	56	77.5
Leucocytes	11,563	11,800
Differential: Per Cent.		
Small lymphocytes	19.5	7.8
Large lymphocytes	5.2	5.4
Polynuclears	57.2	85.6
Eosinophiles	2.3	0.5
Transitionals	2.8	1.

	Highest Count, Dr. Reed.	*Highest Count, This Case.*
Red blood cells	5,264,000	3,900,000
Hemoglobin ......Per Cent.	84	78
Leucocytes	15,500	12,000
Differential: Per Cent.		
Small lymphocytes	36.8	10.
Large lymphocytes	11.5	10.2
Polynuclears	84.28	89.
Eosinophiles	5.	1.5
Transitionals	7.8	1.2

	Lowest Count, Dr. Reed.	*Lowest Count, This Case.*
Red blood cells	2,670,000	3,880,000
Hemoglobin ......Per Cent.	51	77
Leucocytes	6,200	11,600
Differential: Per Cent.		
Small lymphocytes	2.	5.
Large lymphocytes	.8	1.5
Polynuclears	46.4	79.8
Eosinophiles	.05	.2
Transitionals	.6	....

Discussion:

Dr. James Ewing said that he had had the pleasure of looking at the specimens exhibited by Dr. Welch, and considered them one of the most interesting sets of specimens of Hodgkin's disease that he had ever seen. He had been in the situation of seeing a structure which he and, he thought, most pathologists were in the habit of regarding as large round cell sarcoma, but which in fact was not a true sarcoma. He agreed with Dr. Welch that the case was not a lymphosarcoma, and thought, on account of the features brought out by Dr. Welch, that it was in all probability a case of Hodgkin's disease. The tumor itself did not show the gross characters which must be demanded of a malignant lymphoma. It did not show the local destructive and invasive capacities of a lymphosarcoma. Nevertheless the microscopical structure of the tumors in the spinal dura, in the lung, and in the liver, had strongly impressed several pathologists as certainly sarcoma. The question naturally arose: "Under what conditions would one be justified in entering a diagnosis of sarcoma of the lymph nodes?" In this case the rich chromatin content of the cell nuclei of true lymphosarcoma was lacking. Dr. Ewing added that the difference of opinion which had arisen concerning the nature of this case had resulted, in part, because Dr. Welch, who could not perform the autopsy, had not received portions of all the material, while those who had examined the autopsy material had not had the benefit of seeing the sections of the node removed some months before death. He thought that the lesions in the spinal dura, liver, and lung, were strongly suggestive of sarcoma, while the sections of the lymph nodes in Dr. Welch's possession, especially that of the node first removed, seemed to show clearly that the case was one of Hodgkin's disease. Apparently the character of the process had changed, assuming, in some of the secondary lesions, some of the characters of a neoplasm. Dr. Ewing thought it still doubtful whether one would be justified in calling the later lesions true sarcoma.

Dr. W. G. MacCallum had also seen Dr. Welch's specimens, but was forced to admit that he could not yet say what the case was, except that it did not correspond to Hodgkin's disease, unless it was by the greatest stretch of the imagination. Dr. Welch had, moreover, gone to considerable pains to prove that it did not invade the surrounding tissues; but how, then, did it get into the spinal canal? Dr. MacCallum agreed with Dr. Ewing that the tumor did not resemble lymphosarcoma, and that it had not the histological character of a lymphosarcoma. He was of the opinion that it resembled those sarcomata arising in the retroperitoneal region, in which there are large cells of multinuclear character, often with very large nuclei and mitotic figures, which sometimes grow very rapidly and sometimes slowly. On the whole, Dr. MacCallum thought that the case under discussion was one of a neoplasm of slow growth.

DR. KARSNER thought that the case was of interest, especially in view of the publication of two cases by Yamasaki in 1904 (*Ztschr. f. Heilk.*, xxv, 269) which seemed to be of a similar nature. Yamasaki believed that these cases were primarily Hodgkin's disease with sarcomatous transformation. Dr. Karsner had published a case in 1910 (*Arch. Int. Med.*, vi, 175) similar to those of Yamasaki. All of these seemed to be similar to Dr. Welch's case. The condition when it appeared as a new growth was richer in cells than when it occurred in the lymph nodes, showed more giant cells, more large mononuclears, more leucocytes, and fewer lymphocytes, and was definitely invasive. Dr. Welch's case fulfilled these conditions, and it seemed to Dr. Karsner that the case was one of Hodgkin's disease, which had metastasized as an independent neoplasm. This view presupposed the acceptance of the assumption that Hodgkin's disease is a granulomatous condition.

DR. WELCH concluded the discussion by saying that the metastasis was what one would expect in Hodgkin's disease, in that it affected only previously existing lymph nodes which might be anywhere in the body. Dr. Osler had reported a case of paraplegia due to Hodgkin's process in the lymph node in the spinal canal. A superficial examination of these tumors would lead to the conclusion that it was not a case of Hodgkin's disease, but a sarcoma; yet, if he had occasion again to make a diagnosis of a case like this, he would undoubtedly pronounce it a case of Hodgkin's disease. He was of the opinion that a careful study of the development showed that it was not a truly malignant growth, but belonged in the class with the granulomata.

RICKETS.

W. G. MAC CALLUM, M.D.

The disease occurs in different forms in different regions; in some cases there is enough atrophy of the bone to allow of bending at the center and throughout the diaphysis; in others there results a sharp bend in the osteoid tissue at the epiphyseal line. The changes are like those of osteomalacia in certain respects, e. g., the softening and atrophy by way of the production of osteoid substance. The distinction lies in the existence of endochondral changes in rickets which result from its occurrence in the age of maximum growth acitvity.

The changes in the bones of rickets are essentially three:

1. The periosteal growth of new bone and osteoid tissue.
2. The endosteal growth of new bone and osteoid tissue.
3. The endochondral changes.

1.—In many cases there is extensive osteophyte production, thought by some to be compensatory in nature, by others to be set up by the tension of the attached ligaments and tendons. This tissue is similar to the periosteal growth in callus formation, but is relatively slightly calcified, i. e., consists principally in the formation of osteoid.

2.—In the marrow, in relation to the endosteum, there is a change in the tissues (endosteitis fibrosa, osteomyelitis fibrosa) which gives the content of the interlaminar spaces a fibrous character. Laminæ of bone or osteoid tissue are formed by the activities of this tissue, either by the transformation of the fibroid cells into osteoblasts, or by a direct metaplasia. Most of the laminæ may be only partly (centrally) calcified and remain as osteoid.

In both these cases the essential question is as to the production of the osteoid substance—is it a calcium-free apposition, or is it the result of absorption of the calcium salts from the old finished bone laminæ? This question is particularly difficult when the laminæ concerned are in a position (*e. g.*, in the cortex of the shaft) where they may well consist of altered old bone.

M. B. Schmidt is thoroughly in favor of halisteresis and adduces as arguments the existence of calcium-free portions of an otherwise complete and well-calcified Haversian system, the existence of calcium-free ends of lamellæ for a short distance about perforating canals where the rest of the lamellæ are calcified, and, further, the very rapid calcium loss which occurs in the production of such changes. He lays little stress on the *"Gitterfiguren"* of v. Recklinghausen. Marchand supports this view in that there are laminæ with central calcification which, if not formed by halisteresis, must have hung perfectly free in the marrow cavity and there been added to by apposition. Others (Pommer, Schmorl) support the idea of calcium free apposition. Dibbelt rather leans to halisteresis, but the question is far from settled,

3.—The endochondral change characteristic of rickets is found to happen in the following way: at first the invasion of the cartilage by blood vessels is essentially from the marrow cavity, and since calcification of the cartilage, normally present but provisional, occurs in this disease to a far less degree and in irregular areas only, the vessels grow far and branch into the cartilage where it is not calcified, but are restrained where it is. Soon in the florid stage this ingrowth fades into insignificance as compared with the invasion of perichondral vessels from all sides. These arteries and veins which lie in the cartilage marrow canals, grow horizontally and form layers with downgrowing capillaries which later anastomose with those from the marrow cavity. If there are remissions, several such "stages" may be formed. About such vessels there is a sheath of fibrous tissue, and the adjacent cartilage which stains bluish normally, begins to take a pink stain (possibly because of the exchange of a collagenous material for its original chondrin content) and with slight changes in the form of the cells, it assumes the characters of osteoid tissue, a metaplastic process which quite regularly converts whole peninsulas of cartilage into osteoid. Some of the cartilage is simply calcified, and little of it, perhaps none, is converted into real bone in the florid stage of the disease. The enlargement of the epiphyses is due not so much to any excessive production of cartilage as to the fact that it does not become converted into the calcified and less bulky bone.

As to the other organs in rickets, there is no unanimity of opinion. In most cases the spleen is enlarged and there is marked anemia, but this is not held to throw any light upon the pathogenesis of the condition. On the other hand, Stoeltzner attributes the whole change to insufficiency of the chromaffin system, and thinks the lack of adrenalin secretion the fundamental factor in its production. This idea he bases on the observed resemblance to Addison's disease in the atony or hypotony of the skeletal muscles as well as of the smooth muscles of the intestines and arteries. The inadequacy of the adrenalin secretion may be due to the inactivity of the child, for he conceives muscular movements to be necessary to squeeze out the adrenal secretion. Indeed, there have been striking therapeutic effects obtained in osteomalacia by the injection of adrenalin, but their interpretation is not yet quite clear. Similarly Fehling has advanced the theory that the ovaries are in some way responsible for these changes and has produced remarkable cures by their extirpation, but his arguments are easily attacked. Both insufficiency and hyperactivity of the thyroid have been regarded in the same light as causative factors, but on insufficient grounds, and possibly the same may be said for the parathyroids.

In the case presented all of the organs of internal secretion were examined and demonstrated in microscopical preparations, but in none of them could any obvious lesion be seen. Nevertheless it still seems possible that one or other of them may be responsible for the fundamental change in rickets, which is after all not a primary alteration in the nature of the bone, but an inability to make use of the calcium furnished for the process of ossification. It is not as was thought, an excessive production of osteogenic tissue, but rather a retardation or stagnation of the normal bone formation resulting from incapacity to use the calcium supplied.

Studies of metabolism have so far led to quite indefinite results, but whether or not it is greatly increased, the excretion of calcium in rickets is exclusively by the intestine, and Dibbelt puts forward the idea that decomposition products in the intestine withdraw calcium from the blood by producing an insoluble calcium compound within the intestinal lumen.

Discussion:

Dr. Riesman, in discussing Dr. MacCallum's case, said that it was strange that so little should be known of the etiology of a disease that had been studied for so long. Dr. MacCallum had indicated very clearly the pathological anatomy of rickets. The essential change in the disease, as the researches of Pommer and Schmorl showed, was one of deficiency of lime salts. Not alone was the new bone deposited without a proper quantity of calcium salts, but there was a coincident resorption of mineral salts from the existing bone. In some instances, in addition to the changes found by Dr. MacCallum, there had been more or less characteristic alterations in the voluntary muscles. Regarding the true cause of rickets, the speaker said we were no wiser than in the days of Glisson, two hundred and fifty years ago. It was almost amusing to see what varied agents had been blamed for the disease. Some writers looked upon the cause as nutritional, the fats, the proteids, the carbohydrates, and the salts having in turn been accused. Bland and Sutton's experiments seemed to point to diet as an essential factor. Lion whelps fed by him on raw meat and rice developed rickets, but they were cured when milk, pounded bone, and cod liver oil were added to the dietary. The recovery of the lions took place although no change was made in their environment. Monkeys on a purely vegetable diet also became rachitic. Similar observations had been made by Guerin on puppies. It had been held on the strength of the experiments detailed that rickets occurred in the animals because the food was deficient in lime salts. The speaker did not think that such a deficiency could be the cause of rickets. Rickets had occurred in children at the breast of mothers whose milk had been found to contain an abundance of lime salts. Confinement, lack of sunlight, domestication, had something to do with the development of the disease, for, as Holt had shown, the Italian children became rachitic in New York, but not in their native home. Rickets had also been produced in puppies by keeping them tied and confined. Schmorl, one of the best students of rickets, was of the opinion that it was caused by infection. Morpurgo, an Italian, claimed to have produced the disease in young animals by the injection of a diplococcus. As to the adrenalin theory, the speaker hardly thought that the suprarenal gland was at fault. Moreover, Dr. MacCallum had just shown that neither the adrenal gland nor any other organ of internal secretion, was diseased. Recently, however, therapeutic results from the administration of suprarenal extract had been reported. The speaker had lately seen a case of rickets in a child living under ideal conditions. Though the disease was mild, there was a rachitic rosary. It was evident that it was necessary to go further to find the cause of the disease. He was glad that Dr. MacCallum had brought the subject forward so that a new interest might be taken therein, inasmuch as rickets had hitherto been treated as a step-child by pathologists.

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DR. RICHARD M. PEARCE, *President.*

A CASE OF MENINGOCOCCUS ENDOCARDITIS WITH SEPTICEMIA.

RUSSELL L. CECIL, M.D., AND WILLARD B. SOPER, M.D.

Patient, male, stage carpenter, age thirty-one years, admitted to the 2d Medical Division of the Presbyterian Hospital, June 5, 1910, complaining of headache, pain in left arm and chest, lassitude, and fever. Family history negative. Personal history negative, except for immoderate use of alcohol. Patient gave history of two attacks of rheumatism, the first one fifteen years ago, the second, twelve years ago. He was confined to bed several months during both attacks. He had gonorrhea five years ago. No history of lues.

Present illness: Two weeks before admission patient had a sore throat, felt feverish, and noticed some pain and tenderness in right wrist and elbow. Two days later he began to have severe frontal headaches, which continued up to the time of admission. He had vomited a number of times and had some diarrhea. In spite of these symptoms, he continued to work until four days before admission. At that time he began to have a dull pain across the whole anterior chest, which was not increased by the cough that now developed.

Physical examination showed a well nourished man, mentally clear, of good color, but much prostrated. Ear drums normal. Left pupil larger than right, but both react normally. Tonsils moderately enlarged and congested, but without exudate. Neck not stiff. No enlargement of heart made out. Regular action 100 per minute. Presystolic and systolic murmurs can be heard at the apex. Lungs normal. Abdomen soft. Spleen not felt. No petechiae, no Kernig, no Babinski. Knee jerks sluggish. Right ankle somewhat swollen and painful on motion. On the third finger of the right hand, the metacarpo-phalangeal and first interphalangeal joints are swollen, red, and quite tender. Considerable coarse tremor of hands. Temperature 102.5°. Pulse 100. Respiration 32.

Clinical diagnosis: Rheumatic fever and endocarditis.

June 8: The patient's temperature rose to 104.5° and has maintained a level of 102-104.5 . Marked tremor of hands has developed. Patient is quite irrational. Symptoms and physical signs otherwise the same. Leucocytes, 15,000; 86 per cent. of polynuclear leucocytes. The picture is that of an extreme toxemia. The blood culture taken on the day after admission has been reported sterile. Widal reaction negative.

June 9: Patient delirious, with fairly marked subsultus. Leucocytes 12,000 with 90 per cent. polynuclear leucocytes. No petechiae. No signs of meningitis.

June 12: Temperature has continued on a level of 103-

104°. Pulse and respiration have slowly increased, and are now respectively 120-124 and 28-32. Clinically the patient has shown the picture of typhoid fever, except for the absence of rose spots and enlarged spleen. He lies semi-delirious the whole time, having considerable twitching and subsultus. Movements involuntary, but takes fluid greedily. Circulation has kept up well. Blood culture taken on June 9 gave a pure growth of a Gram negative diplococcus, which was reported as probably meningococcus. On the basis of that report patient was given 15 c.c. of Flexner's antimeningitis serum subcutaneously without effect. Patient has had no signs of meningitis.

June 15: Patient gradually failing. Temperature, pulse, and respiration are all rising. The blood culture on June 12 shows same organism found in previous culture. To-day patient received intravenously 15 c.c. of Flexner's serum. Lumbar puncture performed three days ago showed normal fluid. There are now for the first time a few petechial spots, size of pin heads, just beneath the left clavicle.

June 15: Temperature rose to-day to 106°. Delirium changed to coma. Some stiffness of legs and neck, thought not to be that of meningitis. Patient died to-night, circulation having steadily failed despite stimulation.

The autopsy was performed June 16, sixteen hours after death. Only the most interesting features will be referred to.

The body is that of a fairly well nourished young man, 176 cm. in length. Post-mortem rigidity is present. There is livor mortis in the dependent parts.

On opening the abdomen, the liver is found bound to the diaphragm by firm fibrous adhesions. With this exception, the abdominal cavity is negative.

There are old fibrous adhesions in both pleural cavities. The lungs are voluminous and heavy. Their cut surfaces are dark red and ooze considerable blood-tinged frothy fluid.

The pericardial sac has been partially obliterated by fibrous adhesions. The heart with pericardium attached, weighs 670 gms. and is considerably enlarged. The pericardium is peeled off with difficulty, exposing a rough, ragged surface. The right side of the heart contains a post-mortem blood clot. The tricuspid valve measures 12.5 cm. in circumference, the pulmonary valve, 8.5 cm. The leaflets of both valves are normal. There is some hypertrophy of the right ventricle. The mitral valve measures 8.5 cm. in circumference. The two curtains are thickened and fused together so as to form a thick ring. On the auricular surface of the anterior curtain there is a soft cauliflower vegetation, 1.5 cm. in diameter. The base of the vegetation is firmly adherent to the valve leaflet. The aortic leaflets are thickened and pouched out. The free borders of the segments are retracted. The left ventricle is considerably enlarged The papillary muscles are hypertrophied. The musculi pectinati are somewhat flattened. The left ventricular wall measures about 2 cm. in thickness, and has a soft flabby consistence. The musculature is reddish brown and homogeneous. The coronary arteries are clear.

The spleen is large and soft; weight 590 gms. The capsule is smooth. The cut surface is dark purplish red, and has a velvety appearance. Considerable pulp comes away with the knife. The markings are indistinct. Along the anterior border there is a sharply defined pinkish-white area, which on section corresponds to the base of an irregular wedge, firm in consistence, and slightly elevated above the surrounding tissue.

The liver is large and rather soft and pliable. Weight 2,050 gms. The cut surface is pinkish-yellow and opaque. Gall-bladder and bile ducts normal.

The pancreas weighs 200 gms. with duodenum attached, and appears normal.

The right kidney weighs 190 gms. The capsule is somewhat adherent. The surface of the kidney is finely granular. The cut surface is cloudy and swollen, the cortex measuring 10 mm. in thickness in some places. At the upper pole, there is a small pale yellow area surrounded by a narrow zone of red. Section through this area exposes a firm wedge shaped mass of yellow tissue, surrounded by a dark red zone. The pelvis of the kidney is dilated and contains a large rough stone, which sends off projections into the calices. The pelvic mucosa is injected, roughened, and covered with mucus. The right ureter is normal

The left kidney weighs 240 gms. It is finely granular and cloudy like the right. No infarcts occur. Left pelvis and ureter normal.

The suprarenals are normal.

The bladder and prostate are normal.

Nothing of interest is found in the gastro-intestinal tract. The aorta shows no changes. The larnyx and trachea are normal. The brain weighs 1450 gms. The dura mater is normal. The cortex is edematous, but translucent. The sulci contain clear serum. The base of the brain is free from exudate. The ventricles are normal. Frontal sections through entire brain show nothing of interest.

Microscopical sections from the organs showed the following:

Brain: Sections through the various parts of the cortex, as well as the pons and medulla, show a normal pia-arachnoid. Here and there a few lymphoid and plasma cells occur, but nothing suggestive of an exudate can be made out.

Vegetation on Mitral Valve: The vegetation is composed chiefly of fibrin, which in many places has undergone hyaline necrosis. Toward the periphery, the vegetation contains a large number of polynuclear leucocytes, many of them partially disintegrated.

Kidney: The epithelium of the convoluted tubules is cloudy and granular. At one point in the cortex the tubules and glomeruli have undergone a hyaline necrosis. Around this necrotic area, the veins and capillaries are intensely congested.

Spleen: The sinuses are filled with red blood cells. There is a large area of coagulation necrosis, throughout which a network of fibrin is seen. Just outside the necrotic area, there is a hemorrhagic zone. In several of the larger veins passing through the necrotic focus, fresh mural thrombi occur, some of them occupying half or more of the vessel's lumen.

Liver: Cloudy.

Pancreas: Normal.

Suprarenal: Normal.

Heart muscle: There is a slight increase of the interstitial tissue.

Lungs: Normal.

Prostate: Normal.

Anatomical diagnosis: Acute vegetative mitral endocarditis. Chronic mitral and aortic endocarditis. Mitral stenosis, hypertrophy and dilatation of heart. Chronic fibrous pericarditis. Chronic interstitial myocarditis. Chronic fibrous pleuritis. Congestion and edema of the lungs. Acute splenic tumor. Chronic interstitial nephritis. Nephrolithiasis. Anemic infarcts in spleen and right kidney. Cloudy swelling of viscera.

The bacteriological examination of the various organs gave the following: (1) Vegetation on mitral valve. Smears from the vegetation show red blood cells, fibrin, and leucocytes. In some of the leucocytes one to a half a dozen pairs of Gram negative diplococci are found. These organisms are biscuit shaped and show various stages of dissolution. Morphologically, they resemble in every way the diplococcus found in the blood cultures. A culture taken from the surface of the vegetation shows a few colonies of *B. coli communis.*

(2) Smears from the serous fluid beneath the pia mater show a few endothelial cells. No pus cells or diplococci can be found. Cultures from pia mater give streptococci and colon bacilli.

(3) Cultures from liver, spleen, and heart's blood show many colonies of *B. coli communis* and a few colonies of streptococcus.

(4) Smears and cultures from the prostate gland show no gonococci.

In order to establish firmly the diagnosis of meningococcus endocarditis, it has been necessary to prove two premises: First, that the organism isolated from the patient's blood was a genuine meningococcus: Second, that this same organism was instrumental in producing the vegetations on the mitral valve.

(1) Bacteriological study of the diplococcus.

(a) Morphology: The organism isolated from the patient's blood is a small biscuit shaped diploccocus, which does not retain the Gram stain. Morphologically, it resembles the gonococcus. The diplococci vary considerably in size and many involution forms occur.

(b) Cultural reactions: Subcultures, taken from the original broth flasks showed the following: On ascitic glucose agar, after twenty-four hours, there appeared a diffuse, grayish, translucent mucoid growth. On removing some of the growth with a platinum wire, it was seen to have a distinctly viscid quality. Subcultures in broth, plain agar, blood agar, glucose agar, litmus milk, and Loeffler's blood serum, all remained sterile. By making generous transfers, however, from the ascitic glucose agar culture, growths were obtained on all the serum media, and two weeks later the organism was successfully cultivated on plain and on glucose agar.

(c) Fermentation tests: The organism ferments glucose and maltose, but not lactose or saccharose.

(d) Pathogenicity: A guinea-pig was injected peritoneally with one-fourth of a twenty-four hour growth of the organism on glucose agar. It appeared sick on the following day, but completely recovered. This test of the organism's pathogenicity was not carried out until two weeks after its first cultivation on culture media.

(e) Agglutination and absorption tests: An emulsion of the organism in normal salt solution was prepared from a twenty-four culture on glucose agar. The proportion was 4 mg. of the growth to 1 c.c. of salt solution. Two stock strains of meningococcus were used for controls. The three organisms were tested with the serum from a rabbit highly immunized against the meningococcus. Equal parts of the emulsion and of the variously diluted serum were mixed in small test tubes and allowed to stand in the incubator at 37° C. for two hours. They were then placed in the ice box for twenty-two hours. In the positive reactions a flocculent sediment was covered by clear supernatent fluid. In the negative reactions the emulsion remained homogeneous and opalescent. The following table shows the results obtained:

Table No. 1.

Organism	1–10	1–25	1–50	1–100	1–250	1–500	1–1000	1–2500	1–5000	1–10000	1–15000	Salt solution Control
Diplococcus J. S.	+	−	+	+	−	−	−	−	−	−	−	−
Meningococcus Duval.	+	+	+	+	+	+	−	−	−	−	−	−
Meningococcus 250.	+	+	+	+	+	+	+	+	+	+	−	−

Diplococcus J.S., the organism under consideration, was agglutinated by a 1-100 dilution of the serum. The first control strain of meningococcus was agglutinated by a 1-500 dilution of the serum; the second control, the homologous strain, was agglutinated by a much higher dilution, 1-15000.

In the absorption tests, a 1-5 dilution of the serum was first mixed with 1 c.c. of an emulsion of the organism, and the mixture incubated at 37° C. for two hours. Then, after thorough centrifugalization, the clear serum was decanted off, and various dilutions of it were tested with the organisms as in the original agglutination tests. In Table No. 2 the results are seen.

Table No. 2

ABSORPTION OF MENINGOCOCCUS IMMUNE SERUM

Organism	Agglutinative Titer with unabsorbed serum	Agglutinative Titer after absorption with Diplococcus J. S.	Percentage of agglutinins lost by absorption	Agglutinative Titer after absorption with Meningococcus 250	Percentage of agglutinins lost by absorption
Diplococcus J. S.	1–100	1–25	75%	1–25	75%
Meningococcus 250	1–15000	1–5000	66.6%	1–10000	33.3%

The table shows that, after absorption of the serum for two hours with diplococcus J.S., the agglutinating power of the serum was considerably reduced for both organisms. In other words, diplococcus J. S. has the power to absorb specific meningococcus agglutinins. Similar reductions in the agglutinative titer of the serum were observed after absorption with its homologous strain, "Meningococcus 250."

(f) Deviation of complement: In addition to the agglutination and absorption tests, we have also tried the deviation of complement test. The hemolytic system devised by Dr. Noguchi was employed. The antigen was prepared as follows: A twenty-four hour growth of the organism was washed from the surface of a glucose agar slant with 1 c.c. of normal salt solution. The emulsion was well shaken, covered with toluol, and allowed to autolyze over night in the incubator at 37° C. The toluol was then carefully removed, the emulsion centrifugalized, and the clear supernatent fluid pipetted off. For amboceptor we used antimeningococcus horse serum, which was kindly furnished us by Dr. Lamar of the Rockefeller Institute.

There was complete inhibition of hemolysis when 0.01 c.c. of antigen from diplococcus J.S., and 0.05 c.c. of the antimeningococcus serum, were used. With the control strain, inhibition occurred with a slightly smaller quantity of amboceptor, namely, 0.02 c.c. These tests were, of course, controlled with normal horse serum.

The organism showed all the morphological and cultural characteristics of the meningococcus. It was agglutinated by a 1-100 dilution of antimeningococcus serum; finally, it possessed the power of absorbing specific meningococcus agglutinins and of binding complement with specific antimeningococcus amboceptor. We feel justified, therefore, in concluding that the organism was a genuine meningococcus.

(2) Bacteriological Examination of the Vegetations.

In order to show that the vegetations on the mitral valve were caused by the meningococcus, we studied the smears and culture taken at the autopsy, and in addition have cut sections of the vegetation and stained them for bacteria. The smears showed the characteristic Gram negative diplococci in the leucocytes. Only one culture was taken from the vegetation, and that showed a single colony of *B. coli communis.*

Examination of sections through the vegetation reveals many polynuclear leucocytes in a partially necrotic network of fibrin. In many of the leucocytes one to a half dozen pairs of Gram negative biscuit shaped diplococci can be seen. No streptococci can be found in any of the sections of the vegetation.

After having found streptococci in the cultures from the liver, spleen, and heart's blood, it occurred to us that perhaps, after all, we had been dealing primarily with a streptococcus endocarditis, and that the meningococcus was a secondary invader. A careful study, however, of the smears and sections taken from the vegetations have convinced us that the reverse is true. It has been our experience that in streptococcus endocarditis, no difficulty is found in demonstrating streptococci in and on the vegetation. In the present case, we were unable to demonstrate streptococci in the lesion, but were able to find large numbers of Gram negative diplococci in the cellular elements of the vegetation.

The streptococcus and colon bacillus were probably both terminal or post-mortem invaders. Neither of these organisms was found in any of the blood cultures taken. The eighteen hours which elapsed between the death of the patient and the autopsy gave opportunity for extensive multiplication of the colon bacillus in the blood. Its colonies occurred in large numbers in all the cultures, excepting the one from the vegetation.

The absence of meningococci from all the cultures taken at autopsy may be explained in several ways. The low vitality of the meningococcus, and the fact that it is usually intracellular make it a difficult organism to cultivate under the most favorable circumstances. On several occasions we have seen spinal fluids which contained meningococci in the leucocytes, but from which cultures were persistently sterile. Moreover, Flexner found that in the case of guinea-pigs killed by intraperitoneal injections of meningococci, if the autopsies were delayed until partial decomposition of the body had set in, or if the dead pigs had been kept for many hours in the refrigerator, the chances of successful cultivation of the meningococcus were greatly reduced. He explains this in the first instance as probably due to the combined action of inflammatory exudate and the products of decomposition; in the second instance, to the low temperature. The fact that, in our case, the cadaver had been in the mortuary sixteen hours may have been responsible for the negative results obtained.

The second premise may, therefore, be accepted as proved, namely, that the vegetations were produced by the meningococcus.

A CASE OF MULTILOCULAR CILIATED CYST OF THE THORAX.

J. G. HOPKINS, M.D.

The specimen presented was found at the autopsy on the body of a female infant, four days old, dying of bronchopneumonia. On removing the lungs a small tongue-like mass was seen to project into the left pleural cavity from the angle formed by the diaphragm with the posterior thoracic wall and the mediastinum. The mass measured 2 x 1.5 x 1 cm., and was about the color and consistency of a spleen; but on section was found to be rather spongy.

Microscopically the growth was composed of branching acini lined by high columnar ciliated epithelium. In places the epithelium was desquamated in large sheets. The acini contained some coagulated albumin and a few large round desquamated cells. The interstitial connective tissue was very delicate and contained many large sinuses with very thin walls.

The chief point of interest in the case was the origin of this growth. Ciliated cysts of the esophagus have been described, but they have all been unilocular or composed of a few chambers, and have been closely bound to the esophagus. They occur from the level of the thyroid down to the cardia; and many of them have shown smooth muscle and cartilage in their walls. Some unilocular ciliated cysts have also been found in the anterior mediastinum, on the surface of the liver, and in the suprarenals. None of these growths bore a very close resemblance to the one here described. The sections of this tumor strikingly resembled the epididymis, and the irregular arrangement of the acini suggested a rete. In mammalian embryos before the closure of the pleuro-peritoneal membrane the upper pole of the Wolffian body lies very close to the lung, and the Wolffian body begins to regress before this opening is closed. It would seem possible that some of the tubules of the cephalad portion might persist above the diaphragm. The fact that the blood supply of this growth came directly from the aorta by a lateral branch also suggested that it belonged to the urogenital system.

It was possible that sections from other portions of the tumor might throw more light on this question.

Discussion:

Dr. W. G. MacCallum agreed with Dr. Hopkins that the most plausible explanation of the origin of this tumor was that it was an inclusion of some portion of the Wolffian body, which, as is well known, undergoes extensive retrogression later.

A CASE OF CHORIOEPITHELIOMA OF THE BROAD LIGAMENT.

E. MOSCHCOWITZ, M.D.

Dr. E. Moschcowitz demonstrated a case of primary chorioepithelioma of the broad ligament. The patient was a woman, forty-six years old, who had had ten children, the youngest being seven years of age. One year before she had noticed that her abdomen was growing larger; and this enlargement was associated with other manifestations of pregnancy, nausea, enlargement of breasts, etc. The swelling of the abdomen continued for about six or seven months, at the end of which period she was curetted at Montreal, for a reason not ascertainable. The nature of the curettings also could not be determined. The patient was well for two or three months after this, when she began to develop some pain in the left side. On July 1, 1910, she was admitted to Beth Israel Hospital, and on vaginal examination a small mass was found to the left of the uterus anteriorly. There had been absence of menstruation for a month or two before admission, with occasional spotting, and a diagnosis of ectopic gestation was made. An operation was performed by Dr. Ladinski on July 3.

In the left broad ligament there was found a mass about the size of an orange, subtending the Fallopian tube, and having absolutely no connection with the ovary. The left border of the uterus formed the wall on the inner surface of the mass and was involved in the tumor growth. The uterine wall showed absolutely no infiltration. The two layers of the broad ligament formed the anterior and posterior walls of the tumor. Above, the Fallopian tube passed over the mass; below, the growth was in contact with the floor of the pelvis. The ovary was normal in size and position.

On section the tumor was firm, slightly softer in the center than at the periphery. The uterine border was irregular in outline and somewhat honeycombed in appearance. Both layers of the broad ligament were slightly thickened. The tube and ovary were not involved, and there was no loss of continuity anywhere. The uterus was normal in size, shape, and consistency; the uterine cavity was not enlarged, and had been freshly curetted.

The patient returned to the hospital about a month later, with symptoms of generalized malignant tumors of both lungs, and died within two or three weeks.

At autopsy, both lungs were found to be filled with multiple tumors of enormous size. The entire lung was adherent. The rest of the body was entirely free from metastatic deposits, with the exception of the left kidney in which there was a small growth, the size of a penny, near the pelvis. At the site of the stump of the uterus a small mass, about the size of a marble, was found. The nodule on the floor of the pelvis showed very beautifully intravascular extensions of the chorioepithelioma.

Microscopical examination showed chorioepithelioma of the typical type of Marchand. The curettings showed no mole nor any evidence of chorioepithelioma. The picture was that of the "interval" mucosa of Hitschmann and Adler.

Dr. Moschcowitz advanced three possible theories as to the origin of the tumor:

1. That the supposed pregnancy was a hydatid mole, and that the growth in the broad ligament was metastatic.

2. That there was a true pregnancy, and that the chorioepithelioma arose in a chorionic villus that had been projected into the broad ligament.

3. That the tumor arose from a teratoma. Sections taken from various parts showed absolutely no evidence of teratoma. Dr. Moschcowitz was inclined to believe that the first surmise was probably correct.

There was no connection with the tube or ovary. A primary chorioepithelioma of the broad ligament has not been recorded heretofore.

Discussion:

Dr. W. G. MacCallum expressed his interest in the case, inasmuch as he had recently seen two similar ones. The first was in a woman who had been operated on more than a year before, both tubes and ovaries being extirpated. The condition of these organs was not determined. The woman died with symptoms of apoplexy, and at autopsy there was found an apoplectic form of hemorrhage in the cerebral hemisphere, sections of the margins of which showed typical chorioepithelioma tissue. There were similar hemorrhagic areas in the mesentery and spleen, but the uterus showed no changes whatever. The second case was one of well characterized chorioepithelioma developing in the testicle. It would seem that these tumors must be looked upon as a kind of teratoma developing from chorionic structures, which might or might not be connected with pregnancy.

A CASE OF INFECTION BY MUSCA STABULANS.

E. MOSCHCOWITZ, M.D.

The specimens of larvæ were found in the stools of a child, six years of age, who was admitted to Beth Israel Hospital with symptoms of an intense enterocolitis, with bloody stools, diarrhea, fever, and prostration. The fever was irregular, varying between 101 and 103.5 .

On the ninth day of the illness, the larvæ were found in the stools. These persisted for two or three days and then disappeared. The symptoms of enterocolitis, however, persisted, and after a protracted convalescence the child was discharged from the hospital at the end of three months.

Dr. C. W. Stiles, to whom some of the larvæ were sent for identification, reported them as belonging to the Stabu fly. These flies feed by preference on decaying fruits; and the child, who lived in the most unhygienic surroundings, undoubtedly became infected in this manner.

Infections of the intestinal tract by flies are not uncommon. Of the more common species which have been found in human beings, mention may be made of the ordinary fly (*Musca domestica*), the "flesh" flies (*Sarcogaphidæ*), the "flower" fly (*Anthomyia*), and the house fly (*Eristilax*). The symptoms of the infection are those of an enterocolitis. There are a number of reported cases of chronic infection, in which larvæ of flies appeared at intervals in the stools, covering a course of one or two years, Recovery is the rule. In fact, as far as Dr. Moschcowitz had been able to determine, the only fatal case on record was that of Schlesinger and Weichselbaum (*Wiener klin. Wchnschr.*, 1902). In this case a number of irregular ulcers were found throughout the colon.

A CASE OF INFECTION OF THE STOMACH OF THE HORSE WITH GASTROPHILUS EQUI (BOT-FLY).

E. MOSCHCOWITZ, M.D.

Dr. Moschcowitz showed a portion of the stomach of a horse. Numerous larvæ of *Gastrophilus equi* were found closely attached by their cephalic extremity to the mucosa. The vast majority of the larvæ were arranged in a line, just beyond a portion of the stomach in which the mucosa had been completely denuded, showing progressive destruction by the larvæ. The attachment of the larvæ to the stomach was close, and at the site of the attachment there was a round hole surrounding a slightly elevated crater-like projection.

Formidable as the lesion appeared, veterinarians are fairly well agreed that the infection is comparatively harmless. When the larvæ finally mature and are passed by the horse, regeneration of the mucosa takes place. In a few instances, perforation and peritonitis have been reported.

Infection occurs as follows: The bot-fly deposits its egg on the hairs of the horse, preferring the anterior aspects of the body. At the end of four or five days the larvæ break through the operculum and burrow into the skin. This burrowing causes itching, which the horse tries to relieve by rubbing the affected part with the tongue. In this way, the larvæ are swallowed. The larvæ mature in about ten months, usually between the months of May and August. They then pass from the rectum and mature as adult flies in about twenty days.

A CASE OF IMPACTED EGGS IN THE OVIDUCT OF A HEN;

A CASE OF TERATOMA OF THE SACRUM IN A HEN.

E. MOSCHCOWITZ, M.D.

During life the posterior portion of the hen was enlarged to the size of a child's head, rendering locomotion difficult. At autopsy the oviduct was filled with a very hard mass, made up of impacted eggs, which were closely compressed and appeared "hard-boiled." The shells were irregular in outline and were very soft. No stricture of the vagina was present.

The lesion was not uncommon in hens, and was usually found in old hens in whom there was a deficiency of lime in the shells of the eggs.

The specimen of teratoma consisted of a pair of short legs and the pelvis attached to the sacrum.

Discussion:

Dr. W. G. MacCallum said, with regard to the last specimen, that it was not to be regarded as a complete double monster, but rather as a rudimentary inclusion—a parasitic monster analogous to those in human beings in which a portion of an individual was found projecting from the sternum, palate, or elsewhere.

STUDIES ON THE EFFECT OF LECITHIN UPON THE FERMENTATION OF SUGAR BY BACTERIA.

ALBERT A. EPSTEIN, M.D., AND H. OLSAN, M.D.

This work was undertaken with a view to studying the effects of lecithin upon the process of sugar fermentation in vitro. Many functions have been ascribed to lecithin, and considerable discussion has arisen of late concerning its role in metabolism.

It has been assumed by a number of investigators that lecithin exerts an inhibitory action upon the oxidative processes in the animal body.

Diabetes has been claimed in some cases to be due to the inhibitory action of lecithin on the oxidation of sugar. This hypothesis has been chiefly upheld by Luethje, who found that the sugar output in diabetics was usually increased by the administration of egg yolk, a substance rich in lecithin. Bing, as is known, suggested that lecithin and dextrose combined in the blood, forming a substance called jecorin.

Some have even asserted that the alleged decrease in the intrinsic or fundamental metabolism, and the decrease in the oxygen consumption occurring in adiposis, are attributable to the presence of a larger amount of lecithin in the body fluids than that normally present. For example, Kempner and Schepilewsky found that white mice invariably increased in weight after receiving injections of lecithin.

Acting upon this belief, Russian and French investigators have suggested the use of lecithin therapeutically in cases of emaciation and wasting diseases. In support of their claims, the authors quote a number of experiments made upon animals, the results of which do not appear as convincing as the authors believe them to be.

Lately Yoshimoto made a number of animal experiments with lecithin, and instead of finding a diminished output of nitrogen in the urine, he found it to be increased—the increase being the exact equivalent of the nitrogen present in the lecithin administered to the animals. This investigator, therefore, came to the conclusion that lecithin does not exert an inhibitory action on metabolism.

The attempt to ascertain any such function of lecithin in vivo is naturally associated with many difficulties. Even were we to find a diminution in the nitrogen output after feeding lecithin to animals, the conclusion that lecithin produced this result by virtue of its action upon nitrogenous metabolism would not be justifiable. Such a result might be due to an indirect action; for example, we could readily conceive of an increased mobilization of fats produced by lecithin; or possibly even an increased oxidation of sugars, the result of which would be a sparing of proteid material, leading consequently to a diminished output of nitrogen in the urine. This effect would manifestly be, not the result of inhibitory action of lecithin upon nitrogenous metabolism, but the indirect result of an increased combustion of fats and sugars.

The difficulties which arise in the study of a problem of this character in vivo are chiefly due to the fact that it is almost impossible to dissociate a single function or chemical process from every other in the body.

It seemed, therefore, desirable to approach the subject in a somewhat simpler way. Vallet and Rimbaud, as well as Renshaw and Atkins, have recently attempted to solve the problem of the role of lecithin in biological processes, by studying its effect upon the growth of bacteria. Their results show that lecithin does not materially influence the growth of bacteria. However, the method pursued by the above investigators, when taken in conjunction with the object sought after, is not free from criticism. Cellular growth and cellular function should not be confused; the one need not be an index of the activity of the other. The protoplasm of many cell and tissue-forms is endowed with some of the functions present in the living cells. This is true of many enzyme or ferment-bearing cells. The extract of the yeast cell, for example, can ferment sugar as the living cell itself.

Here we have a function that is resident in the cell material and is active even in the absence of cell life. A number of experiments have been made by Kuettner, and also by O. Schwarz, with lecithin and the different digestive ferments. Schwartz, for example, ascribes the inhibitory action of blood serum upon trypsin, to lipoids, presumably lecithin.

We have, therefore, deemed it necessary to take up the study of lecithin in connection with the fermentation of sugars by bacteria. In so doing we deal with a single comparatively simple process in which oxidation plays the chief role. The character of the agents used in the tests to produce the fermentation is also relatively simple.

For our purposes we used three types of bacteria: namely, *Bacillus coli communis*, *Bacillus mucosus capsulatus*, and *Bacillus acidi lactici*. Each of these organisms ferments certain sugars. Our measure of bacterial activity, therefore, was the production of gas and acid.

The amount of lecithin employed in our media at no time exceeded 0.4 per cent. This, of course, is an amount of the substance in excess of that found in biological fluids. If, therefore, lecithin could modify oxidative processes in respect to sugar fermentation, then it would manifest itself by an increase or decrease in the production of gas or acid, or both. We tested the fermentative action of the above bacteria on twelve different types of sugars. This was done to ascertain whether or not the chemical constitution of sugar played any role in the rate and character of its decomposition by bacteria.

The list of sugars includes the alcohol, aldehyde, and ketone type of the different saccharides (mono- di- and polysaccharide.) A hexavalent alcohol and an aldehyde pentose are also represented in the series.

A 1 per cent. solution of each sugar in nutrient bouillon (neutral to phenolphthalein) was used. The media were distributed into fermentation and straight test tubes, 10 c.c. of each medium being used as the unit. To one set of tubes, a 4 per cent. emulsion of lecithin was added, allowing 1 c.c. for each tube. To the other set, sterile salt solution was added in like amount.

Both sets of tubes were inoculated with a loopful of an emulsion of each bacterium and incubated at 37.5° C. All the tests were made in duplicate. A parallel series of uninoculated tubes were incubated and used as controls.

The amount of gas produced in the fermentation tubes was recorded in cubic centimeters at the end of twenty-four and forty-eight hours' incubation. The following table shows the results obtained in tests on gas production:

TABLE 1.—SHOWING GAS PRODUCTION IN CUBIC CENTIMETERS.

		MONOSACCHARIDES			DISACCHARIDES			TRI-SACCHARIDE	POLY-SACCHARIDES		TRIVALENT ALCOHOL	HEXAVALENT ALCOHOL	ALDEHYDE PENTOSE
		Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Bacillus coli communis													
Plain medium	24 hrs	1.0	1.0	1.0	2.0	2.0	0.5	2.0	0	0	0	3.0	1.0
	48 hrs.	1.0	2.0	2.0	3.0	2.0	1.0	2.0	0	0	0	4.0	1.0
Plain medium with lecithin	24 hrs.	1.0	2.0	1.0	2.0	3.0	1.0	0.5	0	0	0	3.0	1.0
	48 hrs.	2.0	3.0	2.0	3.0	4.0	2.0	0.5	0	0	0	4.0	1.0
Bacillus mucosus capsulatus													
Plain medium	24 hrs.	2.0	2.0	2.0	2.0	2.0	0	0	0	0	0	3.0	2.0
	48 hrs.	2.5	2.0	2.0	2.5	2.0	0	0	0	0	0	3.0	3.0
Plain medium with lecithin	24 hrs	1.0	2.0	2.0	2.0	1.0	0	0	0	0	0	3.0	1.0
	48 hrs.	2.0	3.0	3.0	2.5	1.0	0	0	0	0	0	4.0	2.0
Bacillus acidi lactici													
Plain medium	24 hrs.	2.0	3.0	4.0	2.0	2.0	2.0	3.0	0	0	0	3.0	1.0
	48 hrs.	2.0	5.0	4.0	2.0	5.0	4.0	3.5	0	0	0	4.0	2.5
Plain medium with lecithin	24 hrs.	1.0	2.0	2.0	2.0	2.0	4.0	1.0	0	0	0	1.0	1.5
	48 hrs.	3.0	3.0	3.0	3.0	4.0	5.0	2.5	0	0	0	4.0	3.5

SUMMARY.

Bacillus coli communis.

Increased gas.	*Decreased gas.*	*No effect.*
Dextrose	Raffinose	Levulose
Galactose		Maltose
Lactose		Inulin
Saccharose		Dextrin
		Glycerine
		Mannit
		Arabinose

Bacillus mucosus capsulatus.

Increased gas.	*Decreased gas.*	*No effect.*
Galactose	Dextrose	Maltose
Levulose	Lactose	Saccharose
Mannit	Arabinose	Raffinose
		Inulin
		Dextrin
		Glycerine

Bacillus acidi lactici.

Increased gas.	*Decreased gas.*	*No effect.*
Maltose	Galactose	Dextrose
Saccharose	Lactose	Inulin
Dextrin	Levulose	Glycerine
Arabinose	Raffinose	

In the above table we note that with *Bacillus coli communis*, lecithin favors an increase in gas formation in the monosaccharides dextrose and galactose, and the disaccharide lactose; while it inhibits gas formation in the trisaccharide raffinose. The remaining sugars are unaffected.

Lecithin aids gas production by *Bacillus mucosus capsulatus* in the monosaccharides galactose and levulose, while it arrests gas production with dextrose. Lactose and arabinose are influenced in like manner.

With *Bacillus acidi lactici* lecithin also aids the formation of gas in the disaccharides maltose and saccharose, while it checks gas fermentation in all the monosaccharides, excepting dextrose, in the disaccharide lactose, and in raffinose and in mannit. The remaining media are unaffected.

TABLE 2 (*a*)——SHOWING ACID PRODUCTION IN THE DIFFERENT SUGAR MEDIA——IN C. C. OF N/10 NaOH

	MONOSACCHARIDES			DISACCHARIDES			TRI-SACCHARIDE	POLY-SACCHARIDE		TRIVALENT ALCOHOL	HEXAVALENT ALCOHOL	ALDEHYDE PENTOSE
	Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Plain medium—control.......	0.2	0.35	0.7	0.35	0.6	0	0	0	0.15	0	0	0.65
Plain medium Bac. coli com.	7.1	4.6	5.1	4.4	5.2	0	1.05	0.4	0.12	0	4.2	3.60
Net acid produced...........	6.9	4.25	4.4	4.05	4.6	0	1.05	0.4	0.03	0	4.2	2.95
Plain med. Bac. muc. caps....	0.45	0.35	4.3	0.5	0.9	0	0	0	0.02	0	0	0.45
Net acid produced.	0.25	0	3.6	0.15	0.3	0	0.	0	0.05	0	0	0.20
Plain med. Bac. acidi lact.....	4.0	5.5	4.8	7.6	4.9	4.8	4.7	2.85	4.5	0	6.15	7.85
Net acid produced...........	3.8	5.15	4.1	7.25	4.3	4.8	4.7	2.85	4.35	0	6.15	7.20

Table 2 (*b*)—SHOWING ACID PRODUCTION ON THE SUGAR MEDIA IN THE PRESENCE OF 0.4% LECITHIN.

	MONOSACCHARIDES			DISACCHARIDES			TRI-SACCHARIDE	POLY-SACCHARIDE		TRIVALENT ALCOHOL	HEXAVALENT ALCOHOL	ALDEHYDE PENTOSE
	Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Lecithin medium—control	1.75	1.6	1.45	1.4	1.9	0.3	0	0.5	1.35	0.3	0.95	2.0
Culture Bac. coli communis ..	4.5	5.8	7.85	—	6.8	1.2	0	1.85	1.5	0.1	7.55	5.1
Net acid produced	2.75	4.2	5.4	—	4.4	0.9	0	1.35	0.15	— 0.2	6.65	3.1
Cult. Bac. muc. caps	6.1	2.15	8.35	—	2.6	0.5	0	0.35	0.95	0	0.9	4.1
Net acid produced............	4.35	5.5	6.9	—	0.7	— 0 2	0	—0.15	— 0.4	— 0.3	— 0.05	3.9
Cult. Bac. acidi lact...........	9.1	9.4	7.8	12.5	10.5	12.0	9.8	5.3	6.70	—	7.4	9.5
Net acid produced............	7.35	7.80	6.35	11.1	8.7	11.7	9.8	4.8	5.35	—	6.45	7.5

As the above tables indicate, the results of acid production are more uniform than those obtained with gas production. *Bacillus coli communis* causes an increased acid production in the presence of lecithin with all the sugars excepting dextrose and raffinose. With the latter two sugars this bacillus produces less acid in the presence of lecithin than otherwise.

Bacillus mucosus capsulatus produces more acid in the presence of lecithin than otherwise, with all the sugars excepting glycerine and raffinose; upon the latter lecithin has no effect. *Bacillus acidi lactici* in the presence of lecithin produces more acid in all the sugar media.

It is significant that in all the acid tests lecithin has a distinct tendency to increase rather than to decrease the acid production; and if we take acid production as an index of oxidative processes, then we must conclude that lecithin aids oxidation of the sugars.

It is necessary to call attention to the fact that in all our tests lecithin is presumably present in a free state; and although we have reasons to believe from the work done by one of us (E.) in another connection, that lecithin enters into combination with peptone bodies, such as are present in our culture media, we must for the present infer that the lecithin present is in a free state; and the conclusions to be drawn must apply to the action of lecithin present in this state.

To summarize briefly, our conclusions, therefore, are: (1) Free lecithin may modify the bacterial fermentation of different sugars; and hence oxidative processes. (2) The action of lecithin increases the fermentation of some sugars and lessens that of others. There is apparently no definite relationship between the action of lecithin upon the sugars, and their chemical composition.

To sum up: the tendency of lecithin is to increase rather than to decrease fermentation, and consequently oxidation.

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CASE OF RUPTURE OF THE HEART DUE TO CORONARY HEMORRHAGE.*

J. G. HOPKINS, M.D.

This specimen was obtained at autopsy on the body of a woman of fifty years, a designer by occupation. The patient had always been well, except for the diseases of childhood, up to four days before admission to the hospital, when she had a sudden sensation of suffocation while at work and had to be taken home. This attack was followed by rather severe constant pain in the precordia which increased on deep breathing. She had no other symptoms. On examination the apex beat was not made out. The heart dulness was apparently increased; the sounds were distant but normal; no murmurs were heard. The pulse was regular and of good force. After rest in bed the pain disappeared, and on the third day the patient was allowed to sit up, with the expectation of discharge in a few days. While being wheeled to her bed after defecation she became deeply cyanotic, fell forward in her chair, and apparently died instantly.

At autopsy the pericardium contained coagulated blood which formed a thick layer about the anterior, posterior, and right surfaces of the ventricles and extended up about the aorta and pulmonary artery. The clot was thickest at the apex posteriorly, where it measured 2.5 cm. In the apex of the ventricle was a blood clot about 2 cm. in diameter, and in the anterior wall near the septum was a cleft filled with blood clot, continuous with that in the ventricle. This cleft extended downward and to the left, following the course of the muscle fibers. At the left border of the heart it reached the subpericardial fat and extended through the fat communicating with the pericardium apparently at the apex posteriorly, though the precise point of communication was not made out. There was also hemorrhage in the fat below and about the apex of the right ventricle. The ventricles were in complete systole, as is usual in these cases. The left auricle was considerably dilated, and the right contracted or compressed. The valve leaflets were thickened; but on inspection through windows cut in the wall no stenosis or insufficiency could be made out. The coronaries showed extensive sclerosis, and the descending branch of the left coronary was much thickened and diffusely calcareous. The external diameter of this vessel was about 4 mm., but its lumen was very small. About 4 cm. from its origin the lumen was practically occluded by the thickening, and was filled with a thrombus; but could be traced on section 1 cm. or more below this point. The anterior wall of the left ventricle in the region supplied by this artery was pale yellow and appeared necrotic. Microscopically this area showed complete hyaline necrosis of the muscle cells. The thrombus, which to the naked eye appeared to lie in the ventricle, was found to be covered by a layer of endothelium. The blood clot in the ruptured wall was surrounded by large numbers of polynuclear leucocytes. Whereas anteriorly the muscle cells to either side of the hemorrhage were necrotic, posteriorly, near the point of communication with the pericardium, they were fairly well preserved. The aorta showed extensive arteriosclerosis with calcification.

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*From the Pathological Department of St. Luke's Hospital, New York.

There was marked interstitial nephritis. The liver showed chronic passive congestion with extensive deposits of fat and blood pigment. The lungs were emphysematous, markedly congested, and edematous at the bases, and showed some scars of old tuberculosis.

The fact that the blood clot lay beneath the endocardium made it seem probable that this was a rupture due to hemorrhage from the coronary vessels, which extended internally beneath the endocardium and externally into the pericardial sac. The endocardium was intact apparently, and there was no escape of ventricular blood. From the amount of reaction about the clot it was probable that the first hemorrhage into the wall occurred when the patient had her first attack of pain; the terminal event was probably the rupture of this hemorrhage into the pericardium.

The experiments of Cohnheim on increase of fluid in the pericardium showed that a sudden increase of 150 to 200 c.c. was sufficient to cause death, whereas a much larger amount of fluid might accumulate gradually in the pericardium without a fatal result. The effect depends upon the tension of the fluid rather than upon its amount. As the pericardial pressure approaches the pressure in the right auricle it interferes with the entry of blood into the heart from the systemic veins. The pressure in the left auricle is considerably greater than in the right, and consequently the entry of blood from the lungs is not interfered with until the pericardial pressure is increased considerably above the point necessary to compress the right auricle. In the dog a pressure of 60 mm. of mercury was found to be sufficient to block the entry of blood from the systemic veins, causing a rise in venous pressure and a fall in arterial pressure.

In the case reported, the collapsed condition of the right auricle and the dilatation of the left auricle bear evidence that death was due to increased pericardial pressure.

Rupture of the heart is among the rarer causes of sudden death and has aroused much interest since the first case described by Harvey. Morgagni described a number of cases from his own experience, but the lesion appears to be much less frequent in recent times. Elleaume collected sixty-one cases, thirty-seven of which were in men and twenty-four in women. The rupture is usually very minute, as in this case, and usually larger externally than internally. The cleft, as a rule, follows the course of muscle fibers; occasionally there is a long tear—in one case from the base to the apex; and from three to five multiple tears have been reported. Forty-three of fifty-five cases involved the left ventricle, and the usual point was in the anterior wall near the apex. The rupture may follow embolic or sclerotic occlusion of the coronary artery with subsequent softening of the wall. Abscesses in the myocardium, gummata, and tumors have also lead to rupture. Ten of Elleaume's cases were due to rupture of an aneurism of the heart, which is a relatively frequent cause.

Quain suggested that diffuse fatty change might lead to rupture, but this seems unlikely as it lessens the force of the heart action and would rather tend to prevent rupture.

Rupture of the heart occurs in old age and usually after severe exertion. It sometimes occurs without any apparent occasion, and even while the patient is asleep. In other cases it may follow psychical excitement, as in the case of Philip the Second of Spain who died of rupture of the heart when told of the defeat of his armies.

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CASE OF ANEURISM OF THE AORTA WITH RUPTURE INTO THE TRACHEA.*

J. G. HOPKINS, M.D.

The specimen was obtained at autopsy on the body of a German machinist, 59 years of age, who died suddenly shortly after admission to St. Luke's Hospital. He gave a doubtful syphilitic history. He had had no symptoms referable to the aneurism up to one month before death, when he developed a cough with muco-purulent expectoration, which was increased on lying down. About the same time he began to suffer from dyspnea on exertion. The night before admission to the hospital he had a slight hemoptysis.

On admission he was given a bath, and was sitting beside his bed while it was being made up, when he had a severe paroxysm of coughing, brought up several ounces of bright frothy blood, became deeply cyanotic, and died.

At autopsy there was found in the thorax a huge aneurism involving the entire arch and passing without definite boundary into the sclerotic descending aorta. The heart was slightly enlarged and was displaced downward and to the left. When the body was opened the aneurism was collapsed. After distending the sac with very little pressure the ascending portion of the aorta measured 8 cm. in diameter, the transvere portion 9 cm. in its greatest diameter, and the descending portion 4.5 cm. on an average. The inner surface was irregular and covered with raised wheals, and presented numerous hard plaques with beginning calcification. In the posterior wall of the aorta there was a small opening about 2 cm. in diameter which led into a small, comparatively thin wall sac which was adherent to the anterior surface of the trachea. The sac contained a few small thrombi, and beneath one of these, which lay on the posterior wall, there was a small sinus communicating with the trachea just above the bifurcation.

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*From the Pathological Department of St. Luke's Hospital, New York.

The bronchi were filled with blood and the lungs were congested and extremely edematous.

Rupture of an aneurism into the trachea is one of the most common forms of termination, according to Osler, though it is not mentioned in Lebert's series of forty-two cases of rupture. It is not necessarily fatal, and numerous cases of temporary recovery have been reported since that of Zehetmayer in 1845. Premonitory bleedings such as occurred in this case are very common. The large callous cylindrical aneurism probably existed long before the onset of the patient's symptoms. It seems likely that the first symptoms were brought on by the growth of the small saccular aneurism from a thickened part of the posterior wall in the older sac. This is the situation where aneurisms produce symptoms early, the first sign sometimes being fatal rupture into the air passages.

Discussion:

Dr. Wood thought it remarkable that a person could so long survive serious injury to the heart with concurrent hemopericardium. Such severe lesions would usually be thought of as leading to instant death. In a case which he had himself observed, however, the patient, an Italian, had been shot through the sternum, the bullet entering the auricle. After the shooting the man ran two or three blocks down the street to his home and went to bed, where he stayed for two or three days without complaining of anything but slight headache. His family did not know there was anything wrong with him until he died suddenly. At autopsy it was found that the auricle was open and the pericardium filled with blood.

Dr. Louis F. Bishop said that his experience in the hospital with this class of cases was that they had lived much longer than one would think possible when a large amount of blood was found in the pericardial sac. He congratulated the presenter of the specimen upon the beautiful way in which it was prepared, such specimens usually being spoiled by carelessness when they were first discovered.

Dr. James Ewing remarked that an obscure point in these cases was the manner of death. The history of the case under discussion pointed rather distinctly to a sudden onset of symptoms which ought to be accompanied, it seemed to him, by the presence of some signs of recent hemorrhage. He had understood that Dr. Hopkins had not been able to find an area where recent extravasation of blood had occurred. Dr. Ewing had the impression that this clot was all rather old, and that no recent hemorrhage had been found. It seemed to him that in many of these cases it was extremely difficult to determine the cause of death, and a recent experience which he had had seemed to be worth reporting in this connection. A man had suffered a penetrating wound of the chest wall from a long needle about the size of a hat pin, against which he fell, driving the needle through the chest wall and apparently through the heart. He was carried to the hospital, and the house surgeon found nothing but a small puncture over the region of the left ventricle. The needle had been broken off, and the end was just beneath the skin. The patient suffered very severe pain, dyspnea, and shock, remaining in that state for six hours, when he died. The autopsy showed a needle penetrating the wall of the left ventricle, but not entering the cavity. There were six ounces of blood in the pericardial cavity. The heart itself was absolutely sound, except for the trauma. The coronary vessels were sound. The only thing that could account for death was the loss of blood, and apparently the nervous shock arising from the wound.

A CASE OF SCHISTOSOMUM JAPONICUM.

RUSSELL L. CECIL, M.D.

The patient was a Japanese, twenty-eight years of age, who was admitted to the Second Medical Division of the Presbyterian Hospital on November 21, 1910. Five weeks before he had been in Bellevue Hospital for an attack of "fever." The family and previous personal history was otherwise negative; there was no history of gastric disturbances. On the evening preceding admission, after an ordinary dinner, he vomited food and a considerable quantity of bright red blood. This vomiting was repeated once or twice during the night. On admission, about eleven a. m., he was very pale, but free from pain or distress of any kind.

Physical examination showed a spleen reaching to the umbilicus; no other item of importance. During the day the patient was comfortable, but the vomiting of blood recurred during the night, and was repeated a number of times, a total of about forty-eight ounces being raised. He died the following morning about twelve o'clock.

The autopsy was performed on November 23, twenty-five hours post-mortem. The body was that of a young Japanese, and measured 150 cm. in length. Post-mortem rigidity was present; livor mortis in dependent parts. Pupils were equal and moderately dilated. On opening the abdomen, the peritoneal surfaces were smooth and glistening. There were a few adhesions about the appendix, and the neighboring fat contained considerable dense fibrous tissue.

The heart weighed 280 grams. The pericardial sac was normal. The epicardium was smooth and glistening. The tricuspid and pulmonary valves were normal. The aortic leaflets were slightly thickened. There were a few plaques of atheroma at the base of the aorta. The left ventricular wall measured 13 to 15 mm. in thickness. The myocardium was dark brownish in color. The coronary arteries were normal.

The right lung weighed 330 grams; it lay free in the pleural cavity; and its surfaces were translucent and glistening. The tissues were everywhere crepitant. The cut surface was pale. The structures at the hilum were normal. The left lung was collapsed and everywhere adherent to the thoracic wall and the diaphragm. The pleural covering of the lung was considerably thickened, especially along the posterior border, where it formed a thick white dense membrane. The left lung weighed 320 grams with the diaphragm attached. The tissue was resilient and contained very little air. The cut surface was dark and hemorrhagic. The structures at the hilum were normal.

The spleen was greatly enlarged. It weighed 900 grams, and measured 22 x 15 x 8 cm. The surface was pinkish red, and smooth and glistening. The organ had a firm, leathery consistence, and the cut surface was pinkish red and oozed very little pulp. The Malpighian bodies and trabeculæ were prominent. The splenic artery and vein were free from thrombosis.

The liver weighed 1400 grams. It was somewhat smaller than normal, and very firm in consistence. The surface had a pale, grayish brown color, and was coarsely granular, the lobules being separated by irregular fissures of various depths. On the inferior surface of the liver the fissures were deeper than elsewhere and divided the surface into a large number of nodules varying from 0.1 to 2 cm. in diameter. The cut surface of the liver was pale brown and opaque. The normal lobulation had been destroyed, and replaced by lobules of various sizes separated by translucent anastomosing bands.

The gall-bladder contained dark brown viscid bile. The bile ducts were patent. There was no thrombosis of the portal vessels.

The pancreas was pale and firm. On section the lobules were easily separated; a few islands were visible. The pancreatic duct was patent. The lymph nodes surrounding the pancreas was enlarged.

The left kidney weighed 120 grams. The capsule stripped easily, exposing a smooth and pale surface. On section the cortical markings were distinctly seen. The pyramids were sharply defined. The right kidney weighed 110 grams. It was similar to the left in all respects. Pelvis and ureters were normal.

The suprarenal glands were normal.

The bladder was normal.

The rectum contained dark, black tarry material, evidently old blood. There were a few small dark irregularities in the mucosa which had the appearance of healed ulcers.

The mesenteric lymph nodes were not enlarged.

The aorta was elastic and there were a few plaques of atheroma.

The esophagus showed a few dilated and tortuous veins.

The stomach was moderately dilated and contained dark red fluid blood. The gastric mucosa was dark red, glistening, and mottled with small dark spots at many points. At no point, however, was there any break in the mucosa.

The duodenum contained dark reddish brown material.

The jejunum and ileum contained dark red coagulated blood. The mucosa of the small intestine was everywhere smooth and pale. The solitary follicles in the small gut were prominent. Surrounding the head of the cecum there was some dense fibrous tissue which, on section, presented the appearance of a healed focus of some kind. Just below the ileocecal valve there were several small dark red polypoid projections on the surface of the mucosa which had the appearance of polyps.

The large intestine was filled with black tarry material. The mucosa of the large intestine was, for the most part, smooth and glistening.

Microscopical Examination.

Spleen: Sections showed considerable increase in interstitial tissue. The new formed tissue was fairly dense and contained small spindle shaped nuclei. In the interstices of the connective tissue, red blood cells and leucocytes, chiefly of the lymphoid variety, occurred in considerable numbers. The walls of the blood vessels were much thickened, and there was considerable hyaline degeneration in the dense fibrous tissue around them. In many places the red blood cells showed signs of disintegration.

Liver: There was a well marked increase of connective tissue between the lobules and along the courses of the portal vessels. The new formed tissue was dense and infiltrated with considerable numbers of lymphoid cells. There was some regeneration of small bile ducts. At many points in the stroma there could be seen one or more ova lying in the interstices of the tissue; they were oval shaped and surrounded by a thin refractile capsule. Segmentation had occurred in some of the ova. A few of the ova had penetrated into the lobules. Smaller arteries throughout the stroma showed a marked thickening of the intimal coat. The parenchyma was normal.

Pancreas: There was no increase in the interstitial tissue. The islands were rather scarce.

Heart muscle: Normal.

Kidneys: Normal.

Suprarenal glands: Medulla showed post-mortem degeneration. The cortex was normal.

Lungs: The interalveolar septa were congested. Pleura was greatly thickened and hyaline.

Appendix: Normal.

Retroperitoneal lymph node: A small collection of ova, resembling those found in the liver, was found in one of the sinuses. Chyme centers were swollen.

Rectum: Section through one of the small scars showed the following: The mucosa was intact. In the submucosa there was a dense collection of ova similar to those described in the liver. They were separated from one another by connective tissue which showed little or no infiltration. Segmentation had occurred in some of the ova. Small groups of ova occurred here and there in the interstitial tissue of the muscularis. The subserosa also contained small masses of ova. Sections from the ileum and the cecum showed same condition.

Anatomical Diagnosis: Ova of *Schistosomum japonicum* in submucosa of intestine, liver, and retroperitoneal lymph glands. Chronic peritonitis. Splenomegaly. Interlobular sclerosis of liver. Hemorrhages into gastrointestinal tract. Chronic fibrous pleuritis. Atelectasis of left lung.

Schistosomum japonicum infections occur endemically in certain provinces in Japan. They are characterized by enlargement and cirrhosis of the liver, enlargement of the spleen, bloody diarrhea, anemia, and cachexia. Ascites and edema occur in some cases.

As far back as 1888, Majima in Tokio found peculiar ova in the liver of a case of cirrhosis. These he described as the ova of an unknown parasite. It was not until 1904 that Katsurada discovered the parasite in two cats from the province of Yamanaski. These parasites were found in the portal veins and contained ova identical with those previously found in man.

Shortly after this, Fuginami observed several cases, some of them coming to autopsy. He found the ova in the liver, intestinal wall, and mesenteric glands, and also found one of the parasites in a branch of the portal vein.

Morphologically, *Schistosomum japonicum* closely resembles *Schistosomum hematobium*. The distinguishing characteristics of the japonicum are: (1) Its smaller dimensions, only 9 to 12 mm. in length; (2) the larger size of the acetabulum as compared to the oral sucker; (3) the ova, 70 to 75 microns in length, have a smooth capsule instead of one with a spine like that of the hematobium. The ova resemble somewhat those of the uncinaria.

The pathological anatomy of the disease corresponds closely with that found in the case I have reported. The intestinal lesions are chiefly in the large intestine. The wall of the colon is thickened, and there are adhesions about it. Its mucous membrane is swollen and hyperemic, and presents numerous small erosions and patches of necrosis.

The liver is enlarged and hard; its surface is nodular. The mesenteric and retroperitoneal glands are hypertrophied. The spleen is generally quite large and firm in consistence. The urinary bladder is not affected. This constitutes another point of distinction from *Schistosomum hematobium* infection, in which the bladder and genito-urinary tract are involved.

The case reported is evidently a healed case. There were no definite breaks in the intestinal mucosa. The Peyer's patches and solitary follicles were prominent, but there was no ulceration. Many of the ova in the liver showed degenerative changes.

The patient's death was due to hemorrhages following advanced cirrhosis of the liver, the cirrhosis, of course, being the sequel of the schistosomum infection.

Discussion:

Dr. R. M. Pearce said that Dr. A. J. Smith, of Philadelphia, has made a study of what was apparently the first case of this disease in the Caucasian race—an American child living in China. Although Dr. Pearce was not very well acquainted with the facts of the case, he thought it interesting in that so far as Dr. Smith knew no other case had ever been reported in the Caucasian race.

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